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A Record of the Progress of Pharmacy and the Allied Sciences

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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 104 MAY, 1932 No. 5

EDITORIAL

THE COSTS OF MEDICAL CARE

THE Committee on the Costs of Medical Care, "organized to study the economic aspects of the prevention and care of sickness, including the adequacy, availability and compensation of the persons and agencies concerned," continues to function. One of its recent achievements is the publication of a 250-page cloth bound volume "The Costs of Medicines,"* by C. Rufus Rorem and Robert P. Fischelis. The work comprehends a painstaking study of the manufacture and distribution of drugs and medicines in the United States and the services of pharmacy in medical care.

In addition to the array of statistical facts which it presents, it offers as well a considerable amount of "opinion" in the way of authors' recommendations.

With *facts* one cannot differ—but *opinions* are always a challenge.

When the authors state the fact that

> "The annual bill for medicines in the United States is approximately $715,000,000. This is nearly as large as the amounts spent annually for physicians or for hospitals."

We have nothing to say—except perhaps that our national bootlegger bill is tremendously more, and that the bootlegger's poison does vastly more damage than does our annual consumption of assorted medicines. And yet we do nothing about it!!

**The Cost of Medicines; The Manufacture and Distribution of Drugs and Medicines in the United States and the Services of Pharmacy in Medical Care,* by C. Rufus Rorem, Ph. D., C. P. A., and Robert P. Fischelis, B. S., Phar. D. University of Chicago Press. 268 pages. April, 1932. Cloth, $2.50.

They tell us in addition, that

> "More than 70 per cent. of the total expenditure for drugs and medicines is for self-medication, that is, for patent medicines and home remedies. Physicians are writing fewer prescriptions, and the production and consumption of ready-made, packaged medicine is increasing."

To which we react that it is only proof that the right of the individual to self-medicate is inalienable and that unbiased education of the public in matters medical is the real remedy against quacks of all kinds.

And these are not the only facts contained in the volume for this was a research well conducted and quite as well reported. Pharmacists and physicians should carefully read and digest its contents. The recommendations and opinions given in the summary are a challenge to certain branches of the pharmaceutic trade—and as such are bound to find antagonists.

But it can be said, in justice to the authors, that these findings are quite the natural conclusions to the general drift of their work, and they are to be commended on the courage expressed in their summary.

Elsewhere in the pharmaceutical press their opinions have been rather brusquely treated but we do not find it possible to do else here than agree with most of their findings as facts and leave their opinions and recommendations to the customary fate of innocuous desuetude that befalls such presentations.

The summary is herewith appended.

I. More adequate use should be made of the professional knowledge and skill of pharmacists by such methods as (*a*) increasing the opportunities for prescription compounding through elimination of the prescribing of branded products by physicians; (*b*) permitting the instruction of drug store customers in the proper use of medicines which are purchased for self-medication, but not to the extent of diagnosing patients' ailments or recommending medicines based upon description of symptoms; (*c*) arranging for the distribution by the pharmacist of general health information prepared by health departments, both with regard to medicines and general matters of hygiene; (*d*) arranging for the distribution of information to the public concerning the availability of physicians and hospitals, on the basis of lists of physicians provided by local medical or hospital associations.

II. Agencies should be established to prepare and disseminate accurate information concerning the proper use of selected lists of "home remedies" appropriate for self-medication. The lists should be established by a committee of physicians and pharmacists of unquestioned reputation and standing; the distribution of the literature may be accomplished by health departments, hospitals, drug stores, or appropriate lay associations. Universal and unnecessary use of home remedies, "patent medicines," and other self-prescribed medicines should be vigorously discouraged.

III. Secret-formula drugs and medicines should be abolished through the compulsory disclosure on the label of the kind and quantity of medicinal ingredients. Individuals or enterprises which have developed new and distinct preparations should be financially protected by appropriate privileges granted by the United States Patent Office or by a disinterested agency established for the purpose.

IV. All manufacturers of drugs and medicines, regardless of class or kind, should be required to operate under annual licenses to be granted by the federal government upon the fulfillment of satisfactory conditions with regard to competency of personnel, equipment and sanitary surroundings, and standardization of finished products.

IVOR GRIFFITH.

ORIGINAL ARTICLES

INTESTINAL IMPLANTATION OF THE BACILLUS ACIDOPHILUS THROUGH THE FEEDING OF BUTTERMILK CONTAINING ACIDOPHILUS*

By Ivor Griffith, F. A. I. C., Ph. M., and
Morris C. Matt, T. C.

Lacto-bacillus acidophilus, or *Bacillus acidophilus,* was first described by Moro[1] in 1900, thus antedating the discovery of the *Lacto-bacillus bulgaricus* by five years. The latter organism however, was given much more study and attention immediately after its discovery, due to Metchnikoff's characterization of it as the organism predominant in the sour milks consumed regularly by the long-living peasants of the Balkan States. Indeed Metchnikoff[2] actually attributed the longevity of these people to the power of this special buttermilk to arrest intestinal putrefaction, thus "postponing and easing old age."

From time immemorial soured milks from various origins, such as the goat, buffalo, camel, mare, etc., have been a staple article of diet with primitive peoples the world over. In each country the fermenting technic and organism varied somewhat, but the final product was essentially a lactic acid, and sometimes a low alcoholic culture of a living aciduric organism. Thus Norway and Sweden have their Fattemjölk, France, its Gros lait, the Balkan States, Yoghurt (Metchnikoff's pet), Egypt, its Leben raïb, Armenia—Matzoon; Caucasia, its alcoholic Kefir, and Siberia, its Kumiss. Even in the wilds of Africa "Omeira," a Hottentot buffalo buttermilk, is said to have considerable use.

Metchnikoff, however, championed a buttermilk in which the so-called *Bulgarian bacillus* and the *streptococcus lacticus* were the prime inhabitants, and it was on this premise that his experiments were conducted.

This experimental work, conducted at the Pasteur Institute with artificial cultures of the *L. bulgaricus,* convinced Metchnikoff of the possibility of implanting this organism in the intestinal canal of human subjects. Other European workers confirmed his findings to a greater or less extent. Rahe,[3] an American, presented a very complete re-

*A contribution from the Laboratories of the Stetson Hospital.

search on the same subject, differing however, in many respects from the European findings, and actually questioning the possibility of adequate implantation. Bacteriologists have now admitted Rahe's conclusions, and the Metchnikoff bulgaricus theory is no longer seriously considered. Kopeloff, one of the most prolific and dependable workers in the field of aciduric bacteria, thus summarizes in his classic textbook [4] on the subject, his findings in connection with recorded studies of *L. bulgaricus* implantation.

"To recapitulate briefly: it is evident that the question of the implantation of *L. bulgaricus* in the human intestine is the crux of the whole problem of *L. bulgaricus* therapy. The claims made by Metchnikoff are none too convincing when the experimental data are carefully analyzed. Similarly his critics furnish a paucity of substantial evidence. In fact, one is led to believe that the whole matter belongs far more to the category of speculation than that of scientific verity."

Disappointing as this recapitulation is in connection with the *L. bulgaricus,* it is worthy of note that the same author and worker furnishes a much more emphatic and favorable summary of the therapeutic application and value of *L. acidophilus,* a special study of which is recorded in the following pages.

Of *L. acidophilus* therapy, Kopeloff [5] writes: "On the other hand the literature of *L. acidophilus* is sufficiently sound to show that this organism, unlike *L. bulgaricus,* can be easily recovered from the gastro-intestinal tract. The bulk of reliable evidence tends to prove that a simplification or transformation of the intestinal flora from a proteolytic to an aciduric type, dominated chiefly by *L. acidophilus,* may be induced by the feeding of suitable carbohydrates or the ingestion of viable *L. acidophilus* organisms. Direct clinical observations, as well as indirect laboratory methods, have indicated the practical importance of *L. acidophilus* and its therapeutic possibilities.

It remained for the investigators from Yale University [6] (Rettger & Cheplin) to adduce the most important body of information concerning *L. acidophilus* and *L. bulgaricus.* They were successful in implanting *L. acidophilus* in the intestines of animals as well as man, and demonstrated its therapeutic application in certain intestinal disorders."

L. acidophilus is a normal inhabitant of the intestinal tracts of infants, and can always be isolated from the feces of breast-milk fed

infants. Likewise in adults, whose dietary is enriched with milk or milk sugar, it may be quite generally found.

In the adult intestine however, putrefaction and fermentation organisms are greatly predominant, and the view is held by many authorities in this field that the toxic by-products of this bacterial life are absorbed into the blood stream, thus favoring disease and tending to shorten the span of life.

The replacement of this putrefaction and fermentation flora by the milder aciduric type (such as the *Lactobacillus acidophilus*), is suggested as a means of averting such toxic possibilities.

The bacteriologic constants of the *L. acidophilus* are so frequently recorded elsewhere, that they need not be repeated here.

However, the following generalization will not be amiss at this time, namely, that therapeutists and bacteriologists are fully agreed *viable* cultures of the *L. acidophilus* in several types of vehicles and diluents, when administered in proper dosage to animals and humans, are fully capable of implantation in the intestinal tract, with an eventual transformation of the character of the intestinal bacterial flora from a proteolytic to an aciduric predominance.

Additionally it is accepted by the outstanding clinical experimenters, that such implantation is of marked benefit to the average patient, particularly in the alleviation of constipation as well as in the treatment of diarrhoeas.

The only great difference of opinion concerning the administration of this organism has been in the matter of the vehicle or carrier used, and in the manner of its administration.

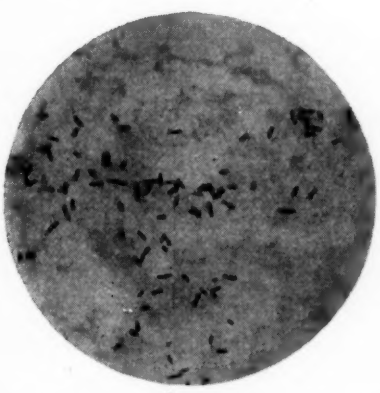
As might be expected, the enthusiasm of certain clinicians in recording their findings, reacted immediately in the flooding of the medicinal market with a host of commercial acidophilus products, many of which were worthless, notably because what bacteria they did contain were dead, and, as such useless. Others contained too few organisms per unit to be of any therapeutic value, and still others contained organisms of related strains but lacking in the specific virtues of *L. acidophilus*.

The particular purpose of this study was to determine, under practical test, whether a carefully controlled blend of pure buttermilk with acidophilus culture of proper concentration, provided an agency wherewith acidophilus therapy might be successfully conducted.

Arguments in favor of a product so manufactured and administered are numerous; its palatability—the ease of its distribution in milk routes, assurance of its freshness when so delivered, and the uniformity of its viable bacterial content.

Metchnikoff had propounded the theory early during his study of buttermilk, that the best implantation and therapeutic results were had by exhibiting the *bacillus bulgaricus* in association with the *streptococcus lacticus* (that is in buttermilk and not in sweet milk).

Proof has been definite that the *L. acidophilus* can be implanted, under certain conditions, in the human intestine, but it remained to be seen whether the association of this organism with the *streptococcus lacticus* afforded a medium which, by symbiotic action, still furthered its implantation and at the same time actually improved its taste.



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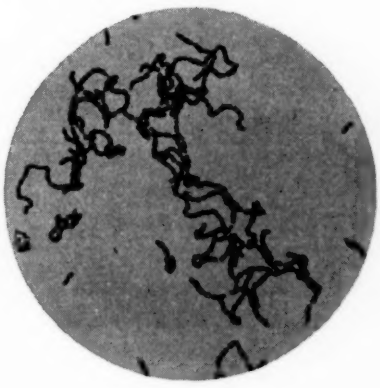

2

PHOTOMICROGRAPHS (mag. approx. 300)
1 *Lacto-bacillus acidophilus.* 2. *Streptococcus lacticus.*

Obviously the crux of such an investigation rests with confirming implantation by isolating from the feces of test humans high counts of the specific type of *L. acidophilus* which was being administered.

Generally speaking the testing was done according to the well established methods of Rettger and Cheplin, and Kopeloff, with modifications where indicated.

Twenty-three patients subsisting on a normal, or at least on their usual diet, were used for the investigation; the tabulated reports however, only indicating the result from eighteen. Five were so inconsistent in their intake of the milk that the findings were judged not to be reliable or informative.

PHOTOMICROGRAPHS - (mag. approx 300.) Showing progressive implantation of L. acidophilus.
1a: Mr. G.B. 4 days after initiation of acidophilus treatment — 1b: 14 days thereafter — 1c: 21 days thereafter.
2a: Dr. R.D. 4 " " " " " — 2b. 7 " " — 2c: 21 " "

The buttermilk containing *L. acidophilus* (X strain) as furnished to these patients, was exactly as supplied to routine users of this already established product, and counts of viable organisms in the buttermilk were as follows:

BACILLUS ACIDOPHILUS ORGANISMS
IN
BUTTERMILK CONTAINING ACIDOPHILUS
USED IN FEEDING EXPERIMENTS

Week of Feb. 28. 1932.

SUNDAY	48 hours old	220 million per c.c.
MONDAY	72 "	184 " " "
TUESDAY	24 "	225 " " "
WEDNESDAY	48 "	204 " " "
THURSDAY	24 "	289 " " "
FRIDAY	48 "	225 " " "
SATURDAY	24 "	262 " " "

Supervision over its actual administration to the patient was as intimate as possible under the circumstances. A pint per diem, in two doses, taken between meals was the regular intake, and to female patients who advanced the objection that it would increase their weight, it was explained that its fat content was but one-half that of sweet milk.

During the first few days of treatment two or three of the subjects experienced symptoms of flatulence and some distension of the abdomen. Continued ingestion of the buttermilk containing acidophilus, with a consequent displacement of the gas producing intestinal bacteria by the aciduric organism, promptly dissipated these symptoms.

In every case one or more samples of feces were examined before the acidophilus treatment was initiated, and twice weekly during treatment. Total bacterial counts were made, and specific counts of the gram-positive acidophilus organism. Counts were also made to determine the gram organism ratios, and all such counts are recorded in the tabular form submitted herewith (group 1 and group 2).

· GROUP · 1 ·

SUBJECT	AGE	FECAL ANALYSIS. — PLATE TECHNIC *Lacto-bacillus acidophilus – x Type* PERCENTAGE OF TOTAL COUNT													RANGE OF PERCENTAGE OF TOTAL COUNT OVER EXPERIMENTAL PERIOD	GRAM ORGANISM RATIOS							
																TOTAL ORGANISMS				GRAM POSITIVE ORGANISMS			
																JAN·14		FEB·4·		JAN·14		FEB·4·	
		1932	JAN. 4.	JAN. 8.	JAN. 10	JAN. 14.	JAN. 18.	JAN. 21.	JAN. 25	JAN 28	JAN. 31	FEB 4	FEB 11	AFTER WITHDRAWAL FEB 25	AFTER WITHDRAWAL MAR 10		% G.P.	% G.N.	% G.P.	% G.N.	% RODS	% COCCI	% RODS	% COCCI
1. MR. G.B.	52		0	0	ADMINISTRATION OF ACIDOPHILUS BUTTERMILK STARTED.	10	12	10	0	32	38	54	49	28	20	10 to 54	14	86	74	26	23	12	58	10
2. MR. L.G.	25		0	0		61	52	48	80	85	88	74	77	52	14	48 to 88	31	69	92	8	18	20	68	18
3. MRS. E.F.	34		0	0		62	91	96	54	58	82	–	80	30	22	54 to 91	18	82	78	22	18	18	62	14
4. MRS. C.H.	42		0	0		18	44	–	82	39	46	52	44	19	10	18 to 82	18	82	80	20	24	14	80	14
5. MRS. A.K.	38		0	–		10	18	–	0	22	30	20	25	5	0	10 to 30	22	78	58	42	20	12	64	10
6. MISS W.E.	22		3	3		–	80	88	72	80	88	80	78	54	24	72 to 88	28	72	64	36	9	19	70	15
7. DR. R.O.	41		0	0		10	14	28	10	60	54	30	48	14	10	10 to 60	35	65	84	16	24	8	56	12
8. MISS G.D.	17		0	0		15	15	52	48	58	40	58	60	52	34	15 to 60	29	61	74	26	20	16	64	18
9. MR. D.R.	12		4	2		80	82	65	85	72	85	80	86	48	40	65 to 86	35	65	76	24	51	11	84	10

KEY–
G.N. = GRAM-NEGATIVE.
G.P. = GRAM-POSITIVE.

The complete technic of both milk and fecal examination is appended in order to place this practical information on record. The results secured from its use proves its trustworthiness, particularly in view of the fact that remarkable checks were frequently achieved during the study. No originality is claimed for either technic or culture materials credit for which rests principally with Dr. W. L. Kulp [7] and associates of Yale University. Some modifications, however, have been introduced, and these have proven quite satisfactory in practice.

A Technic for Estimating Lacto-bacillus Acidophilus in Milk and Feces

Tomato juice agar, a culture medium less complex and much easier to prepare than whey-galactose agar or casein-digest agar, was chosen for the work. This medium shows a marked increase in the size of the *L. acidophilus* colonies and accentuates the X type colony formation.

PREPARATION OF MEDIUM The tomato juice is secured by filtering the liquid portion of whole, canned tomatoes (Montco brand) through coarse filter paper, no suction being used. (Homogenized tomato juice and tomato concentrates have proved unsatisfactory.) To 400 cc. of the filtrate placed in a 1½ liter Florence flask, are added 1.2 per cent. (12 grams) of Bacto agar and 1 per cent. (10 grams) of Bacto peptone. Sufficient distilled water is now introduced to make a total volume of 1000 cc. The agar is then dissolved by placing the medium in the autoclave for 15 minutes at 20 pounds pressure.

ADJUSTMENT OF REACTION Adjustment of the medium to a reaction of pH 7.0, using a La Motte roulette comparator (or any other suitable H-ion apparatus) is carried out on the hot material.

To 10 cc. of the agar plus 1 cc. of Brom Thymol Blue indicator, N/10 NaOH is added, from a certified burette, until the color of the agar matches that in the La Motte Brom Thymol Blue color comparator tube corresponding to a pH of 7.0. From this quantity of N/10 NaOH the amount of N/1 NaOH necessary to adjust the entire liter is calculated. After adding this amount to the liter, and mixing well, a final check is made to insure the accuracy of the work. If necessary, the agar is then filtered through a thin layer of ab-

· GROUP · 2 ·

SUBJECT.	AGE.	FECAL ANALYSIS — PLATE TECHNIC *Lacto-bacillus acidophilus — X Type.* PERCENTAGE OF TOTAL COUNT.													RANGE OF PERCENTAGE OF TOTAL COUNT OVER EXPERIMENTAL PERIOD.	GRAM ORGANISM RATIOS							
													After Withdrawal.			TOTAL ORGANISMS				GRAM POSITIVE ORGANISMS			
		1932	FEB. 4	FEB. 8	FEB. 11	FEB. 15	FEB. 18	FEB. 23	FEB. 26	FEB. 29	MAR. 7	MAR. 10	MAR. 16.	MAR. 24	MAR. 31.		FEB. 15		MAR. 10		FEB. 15		MAR. 10	
																% G.P.	% G.N.	% G.P.	% G.P.	% RODS	% Cocci	% RODS	% Cocci
10. Miss D.B.	42		o	o	ADMINISTRATION OF ACIDOPHILUS BUTTERMILK STARTED.	48	62	59	80	82	–	80	72	38	30	48 to 82	22	78	58	42	20	12	64	10
11. Mr. W.F.	58		o	o		42	18	26	50	58	40	38	54	20	8	18 to 58	30	70	80	20	19	18	70	14
12. Mrs. L.S	62		o	o		5	8	12	–	30	–	18	32	10	2	5 to 32	21	79	52	48	11	11	76	10
13. †Mr. O.B.G.	42		o	o		44	56	52	–	36	58	71	68	40	41	36 to 68	40	60	84	16	23	18	84	14
14. Mrs. R.S.	38		o	–		54	34	–	61	68	54	70	58	28	20	34 to 70	18	82	76	24	14	21	64	13
15 Mrs. R.L.M.	46		o	–		32	38	–	–	58	62	60	68	42	18	32 to 68	32	68	74	26	18	24	68	17
16 †Miss C.C.	16		o	o		54	80	84	80	67	84	80	74	58	56	54 to 84	32	68	80	20	16	11	80	14
17. Miss A.B.	39		o	o		19	24	–	18	27	44	40	40	16	4	18 to 44	10	90	63	37	18	14	72	19
18. Mr. D.F.S.	26		o	o		37	28	20	42	55	39	64	50	52	40	20 to 64	21	79	83	17	12	16	56	11

† Supplementary Lactose (milk sugar) feeding (2 ounces – or 60 gm. daily) started concurrently with the buttermilk & continued after withdrawal of the buttermilk.

KEY–
G.N. = Gram-negative.
G.P. = Gram-positive.

sorbent cotton. Next it is distributed in test tubes in 10 cc. portions, the tubes plugged with non-absorbent cotton and sterilized. The latter is accomplished by autoclaving for 15 minutes at a pressure of 20 pounds. When ready for use the agar is melted in the autoclave as before. The reaction of the finished product should be from pH 6.5 to 6.7.

Estimating the L. Acidophilus Count in Milk Preparations

In estimating the *L. acidophilus* content of samples of milk two dilutions are used, namely 1-100,000 and 1-1,000,000. The apparatus necessary for every sample examined consists of four dilution bottles (the capacity being not less than 120 cc.) of sterile normal salt solution (.0.85 per cent.); two of the bottles containing 90 cc. of the salt solution and two containing 99 cc. In addition two sterile 1 cc. pipettes and two sterile 10 cc. pipettes are required.

With a sterile pipette 10 cc. of the well mixed sample is placed in a dilution bottle containing 90 cc. of normal salt solution, and the bottle shaken vigorously at least fifty times, each shake being an up and down motion of about one foot. This gives a 1-10 dilution. One cc. of this is transferred to the second dilution bottle, containing 99 cc. of salt solution, and this bottle shaken as before. This gives a 1-1,000 dilution. One cc. of this is transferred to the third dilution bottle, containing 99 cc. of salt solution, and the bottle shaken fifty times. This bottle then contains 1-100,000 dilution. Ten cc. of this latter dilution is transferred to the fourth and last dilution bottle, containing 90 cc. of salt solution, and this shaken as the others. The resulting dilution is a 1-1,000,000.

The last two bottles containing the 1-100,000 and the 1-1,000,000 dilutions are used for plating the sample.

PLATING THE SAMPLES

Four sterile Petri dishes and four sterile 1 cc. pipettes are necessary for each sample to be plated. Two plates are made from the 1-100,000 dilution and two from the 1-1,000,000 dilution. To do this 1 cc. of solution is pipetted from the 1-100,000 dilution bottle into one of the Petri dishes, the end of the pipette touching the dish as the liquid runs out. The contents of one of the tubes of agar, which has been melted in the autoclave and cooled down to approximately 100-105 degrees F., is quickly poured over the sample in the dish, and the latter rotated gently to insure thorough mixing of the sample and agar. A second plate is

prepared in the same manner. Finally two plates are prepared from the 1-1,000,000 dilution, following the same technic. It is important that the plating shall be completed as rapidly as possible. When the agar has cooled the plates are inverted and placed in the anaerobic culture jar, indicated in the attached sketch. The best results were obtained by placing not more than four plates in the jar at any one time.

PREPARATION FOR INCUBATION

It has been found that the best growth of *L. acidophilus* on tomato juice agar is obtained by incubating the plates in an atmosphere of 10 per cent. CO_2, the gas being introduced immediately before incubation. The accompanying sketch (Fig. 1), with appended notes, illustrates the set-up for *L. acidophilus* work.

The agar plates are placed in the anaerobic culture jar (J), and the top securely fastened. The inlet tube (I) is connected with a source of CO_2, and the outlet tube (O) with the glass tubing (G), the open end of which is placed in the mouth of the inverted graduated conical cylinder (SR). A Sedgwick-Rafter funnel is employed,

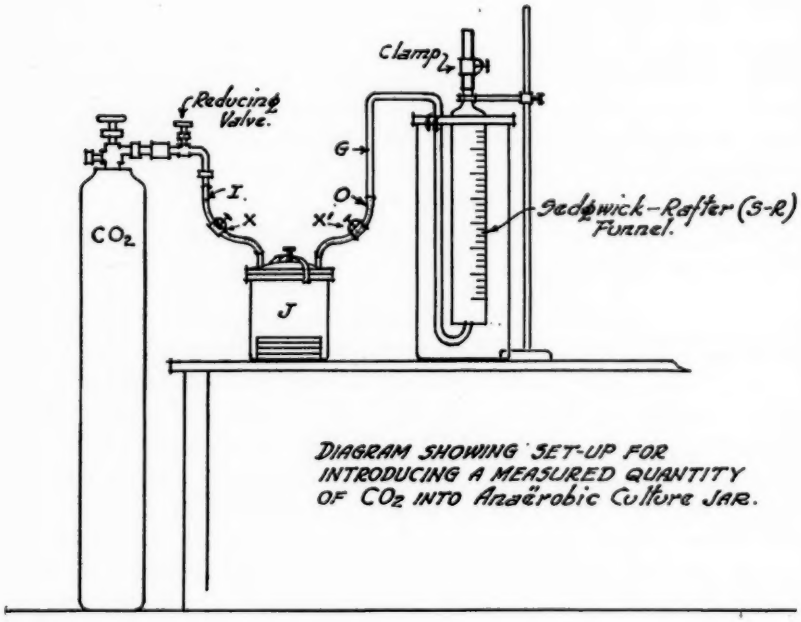

DIAGRAM SHOWING SET-UP FOR INTRODUCING A MEASURED QUANTITY OF CO_2 INTO Anaërobic Culture JAR.

but any large burette or graduated cylinder will serve the purpose. The jar holding the funnel is filled with water.

The volume of the culture jar (J) must be known and can be calculated from the formula: $V = 3.1416 \times R^2 \times L$, where R is the radius of the jar and L is its height. By subtracting from the total volume of the jar, 50 cc. for each dish, the approximate residual volume of the container may be obtained. The clamps X and X′ are opened and CO_2 allowed to enter the container through I, forcing a corresponding amount of the contained air through O. The volume of the displaced water in SR is a direct measure of the expelled air. A volume of water equal to 10 per cent. of the residual volume of J should be displaced by the air forced out by the incoming CO_2. This will leave an atmosphere of 10 per cent. CO_2 in the culture jar. Clamps X and X′ were then tightly closed and the rubber connections disconnected from the CO_2 tank and the gasometer jar. The jar, with plates, was then ready for incubation.

An example of the calculations for displaced air may be of value in making clear the method. Suppose the volume of the jar, calculated by the above formula was equal to 1757 cc., and four plates were to be placed in it. Allowing 50 cc. for each plate we would obtain 1757 cc. minus (4 x 50 cc. or) 200 cc., which would give a total residual volume of 1557 cc. for the jar. We wish to obtain an atmosphere of 10 per cent. CO_2, therefore 1557 cc. x. 0.10 or 155.7 cc. of water must be displaced in SR to produce the desired CO_2 content in the anaerobic culture jar.

The culture jar containing the plates is placed in an incubator, maintained at a temperture of 98-100 degrees F. for 96 hours. At the end of this time the jar is removed and the plates counted.

Estimating the B. Acidophilus Count in Feces

Ten grams of the specimen are weighed into 90 cc. of sterile normal salt solution in an Erlenmeyer flask. This is thoroughly shaken, as was done with the milk samples. Of this 1:10 dilution 1 cc. is transferred by a sterile pipette to 99 cc. of normal salt solution and shaken. Of this 1:1000 dilution, 1 cc. is again transferred to 99 cc. of normal salt solution and shaken. Of this 1:100,000 dilution, 10 cc. are transferred to 90 cc. of normal salt solution and shaken. Duplicate 1 cc. portions of this 1:100,000 dilution and of the 1:1,000,000 dilution are placed in sterile Petri dishes and 10 cc. of melted

tomato juice again poured on as previously described. Incubation is from 4 to 7 days at 37 deg. C.

For the microscopic examination, a small amount of feces is rubbed with a sterile glass rod in a test tube containing from 5 to 10 cc. of normal salt solution until the turbidity approximates tube 12 of McFarland's nephelometer scale (as described in the *J. A. M. A., 49,* 1907, 1176-78) prepared by adding 12 cc. of a 1 per cent. barium chloride solution to 88 cc. of a 1 per cent. sulfuric acid solution Using a "hydrogen-ion block" for comparisons a tube of 0.10 to 0.15 per cent. aqueous solution of potassium dichromate is employed to compensate for the color of the feces. A drop of the fecal suspension is placed on a microscopic slide and Gram-stained according to the special method described herewith.

GRAM TECHNIC Flood the carefully heated fixed slides with distilled water and bring to a boil. DO NOT PERMIT TO DRY AT THIS STAGE. Continue to steam for two or three minutes, then flood with distilled water and drain off.

(2) Flood the slides with dye solution. (Freshly mix 10 cc. of a 1 per cent. solution of Coleman & Bell methyl violet in distilled water, with 2.5 cc. of a 5 per cent. solution of sodium bicarbonate in distilled water.

Allow to stain for five minutes.

(3) Flush off the excess stain with iodine solution (made by dissolving 10 gm. of iodine in 50 cc. of N/1 NaOH and adding 450 cc. of distilled water), and cover with more iodine solution for three minutes.

(4) Drain off the iodine solution, without blotting or water, but do not allow to dry.

(5) Wash the tilted slide with C. P. acetone, using as little as necessary, until drippings are colorless (10 seconds washing).

(6) Air dry.

(7) Counter stain with fuchsin solution (1 gm. of *basic* fuchsin in a liter of distilled water).

(8) Wash with water and air dry.

Summary

(1) It is shown that the gram-positive organisms of *Lactobacillus acidophilus* as exhibited in buttermilk containing acidophilus, are capable of being promptly implanted in large numbers in the human intestinal tract.

(2) It is shown that the daily ingestion of a pint of this freshly prepared product (containing 200 million or more viable acidophilus organisms per cc.) provides ample material for such implantation, and for the continuance of a preponderant acidophilic flora.

(3) It is indicated that the feeding of ordinary milk sugar in addition to the buttermilk containing acidophilus, enhances the implantation factor.*

(4) It is indicated that although there is a gradual diminution of the *L. acidophilus* content of the feces after withdrawal of the buttermilk or any other form of acidophilus treatment a satisfactory implantation may be maintained by the frequent ingestion of lactose or by intermittent treatment with buttermilk containing acidophilus.

(5) It is indicated that while older persons are not as reactive to treatment as are the younger, a successful implantation is quite possible even after sixty years of age.

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*It is interesting to note that through the recent discovery of Dr. Paul F. Sharp of Cornell University there is now available commercially a form of lactose, viz. Beta-lactose, which is considerably sweeter and more soluble than ordinary milk sugar. This product may be used to replace "table sugar" where added lactose is recommended in B. Acidophilus therapy.

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THE CHICK HEART METHOD OF BIOLOGICAL ASSAY

*I. DIGITALIS

By Edith M. Hall

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THE CENTRAL problem of this Institute is the study of the chemistry of cell proliferation. Part of its program is devoted to obtaining suitable test objects for studying the physiological and pharmacological action of any chemical groups which may be significant in cell division. Another part of its program is a study of the effect on growth of the physiological and pharmacological action of various agents.

This report is a step toward finding, at the suggestion of Dr. F. S. Hammett, whether or not the heart of the chick embryo is a suitable test object for such research. The first aim of any such study is a determination of whether or not the response medium can be maintained in a sufficiently stable state to permit repetitive and valid analyses. Therefore a study was made of the utilizability of the chick heart for the assay of digitalis.

The preliminary work was done by Sister Bertha Mueller, to whom I am greatly indebted for technical instruction and advice. It became necessary for her to discontinue the study and it was handed over to and carried through by the author. Valuable suggestions were also made by Dr. F. S. Hammett, of this Institute, and by Dr. Charles E. Vanderkleed, of the McNeil Laboratories, to whom I am also indebted for materials for testing.

Historical

Since the time of Aristotle [1] mention has been made of the embryonic chick heart, but Pickering [2] was probably the first to use it as a test object. He found that the mature heart closely resembles the embryonic heart in its structure and its response to certain drugs (*e. g.*, digitalin and strophanthin). It was his opinion that the heart of the 72-76 hour chick embryo, being free from nerve influence, offered an excellent medium for the testing of those drugs that act directly upon the cardiac muscles. Dareste [3] observed that arrest of heart action was always preceded by arrest of circulation. This was corroborated in the present work.

*The completion of this study was made possible by funds contributed by the McNeil Laboratories.

Our observations in regard to the effect of temperature upon the cardiac rhythm parallel those of Pickering, Fano [4] and Shenk.[5] Fano states, contrary to observations reported by Preyer,[6] that he has never observed the simultaneous contraction of all cardiac musculature. Though this is not a matter directly concerned with the experiment in hand, it is interesting to note that our observations, made in the early stages of the experiment with excised blastoderms mounted on glass slides and observed under a binocular microscope, agree with those of Fano.

Method

After much preliminary experimentation the most satisfactory method was found to be as follows: eggs were incubated in a Sears-Roebuck electric incubator for from 72 to 76 hours. This period of incubation was used because 48 hour embryos are not sufficiently developed to permit satisfactory macroscopic observation, and in the 84 hour embryo the head folds of the amnion often obscure the heart.

The eggs were taken from the incubator, placed on a wooden block having an egg-shaped depression and opened by puncturing the shell over the air chamber. The shell membrane was broken and a small amount of albumen was allowed to escape. A portion of the upper shell was removed. The egg was then placed under the microscope for measuring the posterior vitelline vein and counting the somites. It was then injected with ten minims of the tincture to be assayed and placed in the water bath, where it was observed every 15 minutes until the heart stopped beating.

Repeated tests showed that eggs having from 26 to 32 somites and a posterior vitelline vein 9 to 12 mm. in diameter were most suitable for use in the assay of digitalis. The microscope used for counting and measuring was equipped with a 6x eye-piece and the top lens of a 16 mm. Spencer objective. Since the outline of each somite is well defined by the segmental arteries that run in the intersomitic septa, counting of the somites with the embryo *in situ* is comparatively easy. Measurement of the vein where it emerged from under the embryo was made in tracings of the image reflected from an Abbe camera lucida.

In injecting, care must be taken to avoid three possible sources of error: (1) puncturing a blood vessel, (2) using undue pressure, and (3) injecting the fluid into the amniotic cavity. The best site of injection was found to be just within the marginal vein to the left of

the posterior vitelline vein. Here there is an area comparatively free from larger blood vessels and so far from the heart and amniotic cavity as to minimize possible errors. The fluid should flow gently under the chorion and over the amnion and the circulatory system, thus bringing it in direct contact with the blood vessels and in indirect contact with the heart. Injection of the fluid into the amniotic cavity causes an accumulation of blood-containing fluid in that cavity and cessation of heart action.

The effects of opening and exposure of the egg were found to be negligible. Forty degrees Centigrade proved to be the optimum temperature and this was maintained throughout the test. With decreasing temperatures, heart action gradually slows until at 10 C. it stops. Temperatures above 48 C. cause noticeable increase in heart action.

Since alcohol is the solvent used in the preparation of tinctures, studies of the effects of various concentrations were of importance. It was computed that no tincture in dilution would contain more than 14 per cent. alcohol. Dilutions of 5, 7 and 14 per cent. of alcohol were investigated with results as follows (20 embryos used in each case):

Five per cent. alcohol had no observable effect upon heart action.

Seven per cent. alcohol had no observable effect upon heart action.

Fourteen per cent. produced coagulation of tissues and decrease in heart action, in some cases almost immediately. In a few embryos the decrease was so radical as to take the form of complete ventricular inhibition for as long as 15 minutes. However, out of 20 embryos tested, only one did not recover after the first 15 minutes. All the other embryonic hearts were found to be beating regularly, though slowly, after having been kept in the water bath over night. In the assay of tinctures, we have not as yet found that the alcoholic content affected our final results.

The next step was to see what dilution of a digitalis leaf infusion would give the most regularly appearing cardiac inhibition after a definite interval of exposure. Since some eggs show marked arrhythmias or die after a short period of time even under normal conditions, it was necessary to choose as a period of observation, one long enough to eliminate faulty material. The preliminary work had demonstrated that most of the constitutionally inadequate hearts became markedly irregular in rhythm or stopped beating entirely within the first 30 minutes. The sharpest end point for standardized embryos

was 45 to 75 minutes. If a sufficient number of embryos was used for a test, that dilution of the material being used which caused the greatest number of hearts to stop in the medial period of 45 to 75 minutes was considered "standard". The number of embryos, in other words, the hearts of which did not stop within from 45 to 75 minutes, must be evenly divided, as great a number stopping before 45 minutes as the number that continued beating after 75 minutes. It is of course essential that only embryos with regularly beating hearts be used. The initial rhythm may be from 140 to 190 beats per minute. Any heart showing a marked decrease in heart action within 15 minutes is discarded, except when a strong tincture is being tested. Even with all the restrictions placed upon the embryos to be used, we found that at least 80 per cent. of them were acceptable.

Results

In the first test made with digitalis, a 3 per cent. infusion of the leaf made up in 5 per cent. alcohol was used. Dilutions of 8/16, 6/16, 5/16, 4/16 and 2/16 of this preparation of the drug were tried and 5/16 was found to be the dilution that would stop the majority of the hearts within the specified time. Charts similar to that of Figure 1 were prepared for each dilution. Figure 2 summarizes the results in each case.

In order that a comparison of these results with those obtained by the Official Frog Method of testing Digitalis might be made, this infusion was subjected to the U. S. P. 1 hour frog assay, with a result which corresponded to 90 per cent. of the theoretical 100 per cent. drug. At the same time, the infusion was subjected to the Reed-Vanderkleed Guinea Pig Method of testing and the result obtained indicated a theoretical drug strength of 97.3 per cent. For purposes of approximate comparison, therefore, it may readily be seen that the dilution of 5 parts in 16, which was considered to mark the end reaction in the proposed Chick Heart Method, is the equivalent of 5/16 of 3 per cent. drug strength, which in turn is equal to 15/16 of 1 per cent. drug strength, or is in effect practically 1 per cent.

A comparison of the results obtained by these three methods is contained in the following statement:

For the U. S. P. Frog Test: 0.06 cc. of a 1 per cent. infusion of normal U. S. P. Digitalis Leaf for each gram of frog weight shall stop the heart in systole in one hour.

For the Reed-Vanderkleed Guinea Pig Test: 8.0 cc. of a 1 per cent. infusion of normal U. S. P. Digitalis Leaf when administered to a 250 gram guinea pig shall kill the latter in 24 hours or less.

For the Proposed Chick Heart Method: 10 min. of a 1 per cent. (actually 15/16 of 1 per cent.) infusion of normal Digitalis Leaf shall stop the standard embryo chick heart in not less than 45 nor more than 75 minutes.

A tincture of known strength was then assayed with results as shown in Figure 3. Four unknown tinctures were then assayed with results as given in Figures 4 to 7. A tincture was made from a powdered leaf and assayed (see Figure 8).

From these assays a table of percentages was compiled (Figure 9). This table was checked by the following method: the original tincture No. 5979 was diluted to one-half. Since it had taken 7 per cent. of the orginal drug in dilution to produce the required results, we calculated it would take 14 per cent. of the dilution of half drug and half diluent to produce the same effect. Fourteen per cent. of the drug in dilution was tried and the results were as follows (Figure 10): Since it had taken twice the amount of drug in dilution to produce the desired effect, therefore the drug was exactly one-half as strong as the original. In this way the accuracy of the present method of assay was checked.

FIGURE 1

5/16 OF A 3% INFUSION IN DILUTION (5 CC. INFUSION AND 11 CC. 5% ALCOHOL)
(X INDICATES CARDIAC INHIBITION)

Egg No.	At Opening	From 0-15′	From 15-30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
	Number of Heart Beats per Minute						
1	174	116	112	38	X		
2	158	110	100	62	66	50	..
3	154	126	126	126	76	58	..
4	166	140	92	36	X		
5	180	148	144	120	16	X	
6	170	148	24	10	X		
7	164	112	108	114	36	X	
8	160	140	122	120	38	X	
9	162	118	72	18	X	..	
1	182	128	130	62	34	X	
2	176	128	128	86	76	64	..
3	188	170	120	80	56	X	
4	180	162	146	50	X		
5	170	150	140	54	50	X	
6	180	162	64	X			
1	148	120	116	118	72	60	..
2	176	128	96	76	34	X	
3	170	144	82	32	X		
4	170	148	80	12	X		
5	152	136	138	22	X		

FIGURE II

INFUSION

3% Inf. in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
8/16	20	7	9	3	1	0
6/16	19	4	8	4	0	3
5/16	20	0	1	8	7	4
4/16	20	1	5	2	5	7
2/16	20	0	0	2	1	17

FIGURE III

TINCTURE #1 (KNOWN STRENGTH)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
8%	20	9	7	2	1	1
12%	20	5	3	4	3	5
13%	20	3	6	4	1	6

83%

(assayed 109% Frog Method)

FIGURE IV

TINCTURE #2 (UNKNOW STRENGTH)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
10%	20	3	3	2	1	11
15%	20	2	5	4	4	5
25%	20	8	5	3	0	4

66 2/3%

(assayed 73% Frog Method)

FIGURE V.

TINCTURE #3 (UNKNOWN STRENGTH)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
15%	20	0	1	6	1	12
20%	20	3	2	4	4	7
25%	20	4	2	6	1	7
30%	20	11	5	2	0	2

50%

(assayed 54.5% Frog Method)

FIGURE VI

TINCTURE #4 (UNKNOWN STRENGTH)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
10%	10	8	1	0	1	0
8%	9	3	3	1	0	2
7.75%	10	0	2	3	2	3
7.5%	10	0	0	5	2	3

129%

(assayed 109% Frog Method)

FIGURE VII

TINCTURE #011929 (UNKNOWN STRENGTH)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
10%	10	6	1	3	0	0
12.5%	10	2	3	1	1	3
15%	10	0	3	2	3	2
20%	10	0	0	3	2	5

66 2/3%

(assayed 77% Frog Method—74.3% Guinea Pig Method)

FIGURE VIII

TINCTURE #5979 (MADE FROM POWDERED LEAF)

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
10%	10	6	1	3	0	0
7.5%	10	2	3	1	1	3
7%	10	0	3	2	3	2
5%	10	0	0	3	2	5

143%

(assayed 153% Frog Method—133% Guinea Pig Method)

FIGURE IX

TABLE OF PERCENTAGES

Drug in Dilution	Normal Activity
5%	200%
5.5%	182%
6%	166 2/3%
6.5%	154%
7%	143%
7.5%	133 1/3%

8% 125%
8.5% 118%
9% 111%
9.5% 105%
10% 100%
10.5% 95%
11% 91%
11.5% 87%
12% 84%
12.5% 80%
13% 77%
13.5% 74%
14% 72%
14.5% 69%
15% 66 2/3%
20% 50%

FIGURE X

TABLE SHOWING METHOD OF CHECKING RESULTS

TINCTURE #5979

Drug in Dilution of	No. Hearts Observed	Number of Hearts Stopped in: Less Than 30′	From 30-45′	From 45-60′	From 60-75′	Over 75′
(143%)						
7%	10	0	3	2	3	2
(72%)						
14%	10	2	1	2	2	3

Summary

The suitability and practicability of the heart of the 72 to 76 hour chick embryo as a test object for the bioassay of digitalis has been demonstrated.

The standards adopted for grading the embryos are discussed.

Results of the assays are compared with those obtained by two other methods.

The method described permits of accurate checking of results.

Conclusion

A new method for the biological assay of digitalis is proposed, using the heart of the 72 to 76 hour chick embryo as the test object. Certain obvious advantages of this method are: the economy, convenience and constant availability of the material; the ease with which

the assay may be made; the smaller number of variable factors in the organism tested; the accuracy with which results may be checked (*cf.* Figure 10).

Results obtained compare favorably with those obtained with the U. S. P. Frog Method and the Reed-Vanderkleed Guinea Pig Method.

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"COLLOIDS: A STORY ABOUT PARTICLES"*

By Arthur Osol, Ph. G., M. Sc.

IN THIS modern age of intensive scientific specialization, a lecture on colloids and colloidal chemistry would hardly seem to be a suitable subject for a popular science talk. Yet this apparently specialized field of investigation is more general in its applications than general chemistry and more intimately concerned with our daily routine than we have reason to believe.

Arthur Osol, Ph. G., M. Sc.

Before giving a formal definition of the term colloid let us briefly consider several common experiments. When sugar is placed in water it dissolves and becomes uniformly distributed throughout the solution. The process of solution probably consists of the subdivision of the sugar granules into particles so small that they cannot be seen with the strongest magnifications. These very small particles are called molecules and are considered to be the smallest bits of sugar which can exist by themselves. The average diameter of a sugar molecule is probably about 0.00000004 of an inch. Small wonder that we cannot see it, for our highest magnifications render visible only those particles which are larger than 0.00001 of an inch.

Why do the sugar molecules remain uniformly distributed in the solution? Science tells us that a substance like water, which outwardly seems to be at rest is really a seething mass of millions of impetuous and jostling molecules, always bumping into each other and into any foreign molecules which may be present. Imagine then the predicament of the sugar molecules in the midst of such an unruly crowd. They are bumped in one direction or another until very shortly they are quite uniformly distributed among the water molecules and in turn help to keep themselves distributed by colliding with other molecules.

If on the other hand a substance-like clay is placed in water it is found sooner or later that the clay settles to the bottom of the container. If we examine the clay as it settles we have little difficulty

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discerning the individual particles. These particles may be thousands of times larger than the smallest particles of clay which could exist by themselves. It is appropriate to inquire why the clay particles are not bumped hither and yon by the water molecules instead of settling to the bottom of the container. Actually they receive as many and more bumps than any molecule of sugar, but when we recall that the particles of clay are much larger than the sugar molecules, we would hardly expect them to be very much affected by the collisions and accordingly they must obey the universal law of gravity. The objection might be raised that gravity also acts on the sugar molecules and should pull them down likewise. Such a tendency does exist, but before the molecules of sugar have much chance to settle they are bumped far off their downward course.

If our theory is correct it should be possible to show that the finer the clay particles the longer will they remain suspended in water. This fact may be easily tested by making suspensions of clay of varying degrees of fineness and determining the length of time required for the particles to settle. Actual experiment shows that if the clay particles are fine enough, weeks may elapse before they settle. If we were to examine such a mixture we would no longer be able to see the individual particles without considerable magnification. Under a high-powered microscope, however, a most interesting phenomenon is observed. The smaller particles of clay, now made visible, are seen to be moving in all directions, the smaller the particle the faster the motion. This motion is called "Brownian movement" after the English botanist, Robert Brown, who first observed it. The average diameter of the smaller particles of clay which exhibit Brownian movement is not very much above the lower limit of microscopic vision, namely 0.00001 of an inch, or approximately 250 times the average diameter of a sugar molecule.

This evening our discussion will be centered on the behavior of particles intermediate in size between molecules and very fine particles which are barely visible under the ordinary high-powered microscope. In this range of subdivision of particles many interesting and peculiar properties are exhibited.

In 1861 Thomas Graham introduced the name colloid to designate substances in this fine state of subdivision, the name being derived from a Greek word meaning glue. Although glue is a typical colloid, we should be careful not to gain the impression that colloids are substances related to glue. As already shown, a colloid represents a par-

ticular physical state which may, under the proper conditions be assumed by any compound. Thus even the very soluble sodium chloride, which we know better as table salt, has been prepared in the colloidal state.

The original definition of a colloid was based on Graham's experiments on the diffusion of substances through various semi-permeable membranes such as hog's bladder, goldbeater's skin, collodion bags, etc. As shown diagrammatically in Figure 1 these membranes are permeated with very small openings or pores, so small that most particles of colloidal dimensions cannot pass through them, yet large enough for the passage of a molecule of sugar, for instance. The substances which diffused by this operation of dialysis, as it is commonly known, were called crystalloids by Graham, while substances which did not diffuse were called colloids.

This distinction between colloids and crystalloids has been dropped as a result of modern developments in colloid chemistry. It has been shown, that membranes may be obtained with pores so small

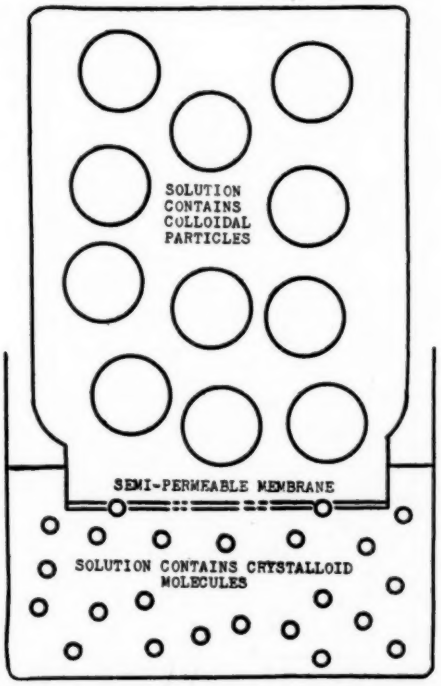

Fig. 1—Dialysis Showing Separation of Colloids From Crystalloids.

as to retain molecules or large enough to allow some colloids to diffuse through. Again, since it is possible to prepare most substances in a colloidal state, the distinction between crystalloids and colloids loses most of its significance.

It would seem from our discussion thus far that colloidal particles are necessarily particles of solids. Although the properties of solids were the first to be studied in the development of colloid chemistry, the similarity of the behavior of small volumes of gases and liquids justified their inclusion in the realm of colloid chemistry. Thus Bancroft gives a very flexible definition that colloid chemistry is the chemistry of finely divided or dispersed bubbles, drops, grains and even filaments and films. The inclusion of the last two may be somewhat surprising, but on careful observation we find that the properties of both filaments and films depend on the smallness of at least one of their dimensions.

As an example of a gas in the colloidal state we have but to recall the "fire-foam" type of fire extinguisher. The use of this device depends on the formation of a stabilized carbon dioxide froth in which the bubbles are very finely dispersed. Before the present era of prohibition it would have been proper to cite the foaming of beers as an excellent example of gas bubbles in a fine state of dispersion. Still another example of colloidally dispersed gas is found in the mineral meerschaum in which notable quantities of gas are present.

Perhaps the best examples of finely divided liquids are found in the class of emulsions of water and oil. As shown diagrammatically in Figure 2 two types of water and oil emulsions are possible, de-

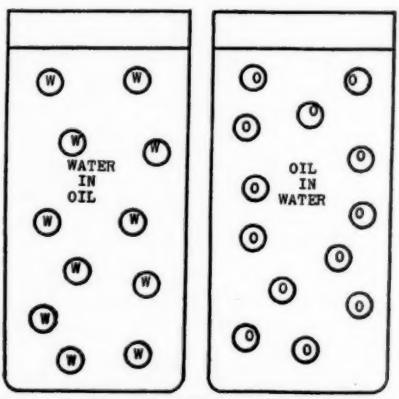

Fig. 2—Types of Emulsions of Water and Oil.
W = Water; O = Oil.

pending on whether the oil or the water is finely dispersed. Milk is an example of an emulsion in which fat particles are dispersed in a water base, cod-liver oil emulsion being another example of the same type. The water in oil type of dispersion is best illustrated by butter, in which the water is present in minute droplets.

It is likewise not necessary that water nor any other liquid be the medium in which substances are finely dispersed. Fog is a colloidal dispersion of tiny drops of liquid in a gas, while smoke consists of small particles of solid suspended in a gas. Again, various stones are colored by the presence of finely dispersed pigments, an example of a solid dispersed in a solid.

Properties of Colloids

It has already been pointed out that colloidal particles of clay suspended in water are constantly moving about in all directions. This motion is characteristic of substances in the colloidal condition, the smaller the particles the faster being the motion. In many cases this motion can be directly observed with the aid of a high-powered microscope, but for those particles which are so small that they cannot be seen with an ordinary microscope it is necessary to use an instrument known as the ultra-microscope. The principle underlying the use of this device is based upon a commonly observed phenomenon. All of us have noticed that dust particles in the atmosphere which are ordinarily invisible can be readily seen if a narrow beam of light is passed through the atmosphere. The visibility is due to the scattering effect on light by the small particles of dust. An identical effect is observed when a beam of light is passed through a solution containing colloidal particles while with true solutions of substances such as sugar, salt, etc., the path of the light is invisible. This phenomenon is known as the Tyndall effect and is another of the characteristic properties of the colloidal particles. If the beam of light as it passes through a solution of a colloid is examined from above with a microscope it is possible to see scintillating flashes of light which are reflected, refracted or scattered upward by the very small particles, although the particles themselves cannot be seen. The ultra-microscope is constructed on this principle (see Figure 3).

AREA

As particles are made smaller and smaller by continued subdivision it is evident that additional surface is being formed. In order to show the increase of total surface area by continued subdivision of a cube, originally one inch on a side, the following table is given:

TABLE I

VARIATION OF AREA WITH PROGRESSIVE SUBDIVISION

Length of Edge	Number of Cubes Formed	Total Area
1.000 inch	1	6 sq. in.
0.100 inch	1,000	60 sq. in.
0.010 inch	1,000,000	600 sq. in.
0.001 inch	1,000,000,000	6000 sq. in.

This information in itself would be uninteresting were it not that nature has invested substances with certain properties which vary as the amount of external surface or area. In general all substances have a certain ability to adsorb other substances in contact with it. The term adsorb should not be confused with the very similar name

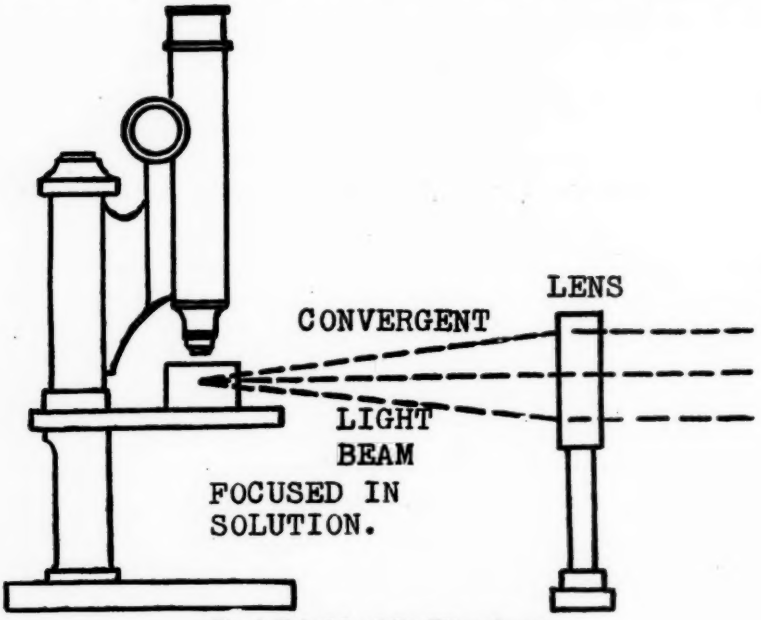

Fig. 3—Principle of the Ultra-microscope.

absorb. A sponge absorbs water, *i. e.*, it takes up water within its pores, but a substance which adsorbs another material is attached to the latter primarily by surface attraction. Thus certain dyes like the indigos and blacks, are considered to be adsorbed on the surface of colloidal silk and wool fibers.

ELECTRIC CHARGE

Nearly all colloidal particles have been shown to carry charges of electricity which may be either positive or negative in character. This fact may be verified by passing a direct current through a solution of a colloid, if the latter is charged positively it gradually migrates to the negative pole, while if it is charged negatively movement toward the positive pole takes place. This phenomenon is known as cataphoresis (see Figure 4).

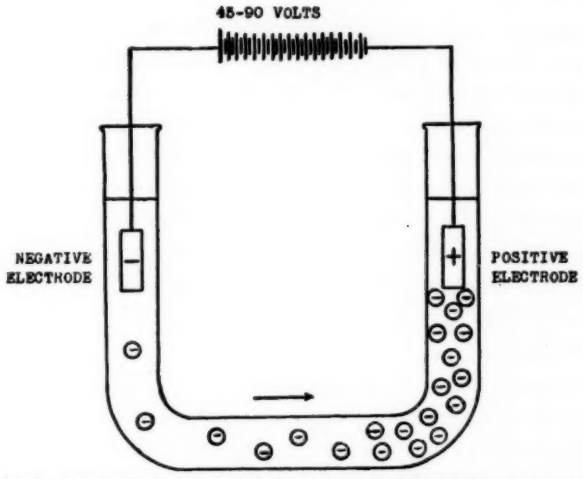

Fig. 4—Cataphoresis in a Solution of a Negatively Charged Colloid.

REVERSIBLE AND-NON-REVERSIBLE COLLOIDS

Although the colloidal state may be exhibited by any substance, it is possible to distinguish between substances which possess a natural tendency to remain in the colloidal condition and those which do not. Certain colloids like glue and gelatin exist normally in the colloidal state and it is possible to evaporate solutions of these substances to dryness and again obtain them in the colloidal state by adding water to the dry residue. Such substances are designated as reversible colloids. Still other substances such as colloidal arsenic sulphide and

other metallic sulphides will not form a colloidal solution after evaporation to dryness and addition of water. The latter are known as irreversible colloids.

COAGULATION AND PEPTIZATION

All of us are more or less familiar with the significance of the term coagulation. Substances in the colloidal state very often can be precipitated so that the individual particles become quite large. The term coagulation is applied to this precipitation of colloidal substances in the form of larger aggregates. With the formation of larger aggregates the characteristic properties of the colloidal state which are due to size immediately disappear. The reverse operation, *i. e.*, that of dispersing the larger aggregates into smaller ones is known as peptization.

Colloids may be coagulated by the addition of various chemicals or by the passage of a high tension electric current. Coagulation of colloids may be very nicely shown by adding an acid to a colloidal solution of arsenic sulphide. Before the addition of the acid the solution is golden yellow in color, perfectly clear if freshly prepared, but upon the addition of an acid, comparatively large particles of arsenic sulphide are seen to form. The explanation of this coagulation probably depends on the neutralization of the charges of electricity on the colloidal particles by the charges carried by the ions of the acid. That this is true in some cases at least may be demonstrated by the precipitation of negatively charged colloids by the addition of colloids carrying a positive charge.

PROTECTIVE COLLOIDS

When silver nitrate is added to a solution of potassium iodide, a new substance, silver iodide, is formed. This substance belongs to a class of compounds which are insoluble and ordinarily settles out after a few minutes leaving a fairly clear supernatant liquid. If, in this experiment, small quantities of gelatin solution are added to each of the two solutions, the precipitate remains suspended for a very much longer time and the individual particles of silver iodide are much smaller. The gelatin acts here as a "protective" colloid in preventing the precipitation of silver iodide in large masses which are formed when no gelatin is present. Any colloid which acts in a similar manner is "protective" in nature, and as a general rule the reversible colloids are also "protective".

Practical Applications of Colloids

An attempt to include all the practical applications of colloid chemistry would be futile, for the story is far from being complete. Let us first consider some of the colloidal aspects of life. Life consists of a series of complicated chemical reactions, the speed with which these are consumnated determining the state of our health and welfare. Most reactions are either fast or slow, depending as a rule on the degree of subdivision of the reacting substances. The rate of digestion of food depends on how fine the individual food particles are when they reach the stomach. Particles which are too large require a long time for digestion and if they are extremely large the process becomes so slow that putrefaction with its attendant discomfort sets in to inform us that the chemical laws of nature dare not be disobeyed. The importance of maintaining proper particle size of the colloids which compose our body is excellently stated in the following excerpt from Alexander's book on Colloid Chemistry: "Figuratively speaking, if all chemical substances comprising our organism were in true or crystalloidal dispersion, reactions would proceed so rapidly that we would, so to say, live ten years in ten minutes. On the other hand, if coarse dispersion prevailed, it would take ten years to live ten minutes. Every organism is dependent upon the co-ordination of its chemical reactions in point of time, and this leisurely procedure depends largely on degree of dispersion, which keeps chemical reaction velocities within certain speed limits."

It is significant that many cases of insanity have been shown to arise from a disturbance of brain colloids. Some cases are the result of over-coagulation of these colloids while others are caused by excessive peptization or over-dispersion of the same colloids. Dr. Wilder D. Bancroft, the eminent colloid chemist of Cornell University, has experimentally proven that complete cure or at least definite improvement of cases of insanity have followed upon a treatment designed to correct the disarranged brain colloids.

The colloidal nature of antitoxin—toxin reactions may be demonstrated by observing them under an ultra-microscope. Thus tetanus antitoxin and toxin mutually precipitate each other, as do diphtheria toxin and antitoxin.

COLLOIDAL PREPARATIONS IN MEDICINE

Many preparations have been introduced to the medical profession which are essentially metals in colloidal dispersion. Thus colloidal silver has been applied in the treatment of diseases of the respiratory tract as well as

in cases of meningitis, typhoid fever, cholera, malta fever and rheumatism. Colloidal gold, platinum, palladium and rhodium have also been used in many of these diseases. Colloidal mercury has been used in the treatment of syphilis. Selenium, iron, manganese and sulphur in colloidal solutions have found some application in the treatment of various disorders. Colloidal arsenic sulphide has been reported to be of value in the treatment of trypanosomiasis. The use of colloidal palladium oxide has been reported in cases of obesity. The treatment is said to consist of hypodermic injections of the material into the fatty areas which are to be reduced in size.

THE WEATHER Variations in climatic conditions depend to a large extent upon the degree of dispersion of water in the atmosphere. Water, continually evaporated from bodies of water, condenses upon dust particles to form clouds. If the clouds come in contact with cooler regions in the earth's atmosphere, larger and larger particles of water are formed until rain finally precipitates.

Colloidal particles of ice suspended high in the earth's atmosphere are the cause of the formation of halos. One of the most unusual of these was seen in Philadelphia in May, 1915, being visible for approximately two hours. The formation of the halo arises from the refraction of light by ice particles.

The blue color of the sky, as well as the vivid colors of sunset are caused by the diffraction of sunlight by dust particles present in the atmosphere. Although dust is the bane of all whose business it is to keep house, we would find this world a very gloomy and poorly illuminated place to live in if dust particles were not continually present in the atmosphere. In a sky free of dust particles the sun would stand out as a shining ball of fire in a black, star-studded sky. Of course, the presence of too much dust localized in one place has the effect of absorbing the beneficial ultra-violet rays.

The prevention of industrial smoke in large cities has been the subject of many investigations. Various methods have been suggested to eliminate this annoyance, the one of particular interest to us being the removal of the colloidal dust particles present in gases by the passage of a high tension electric current. Cottrell was the first to devise a successful electrical precipitation method, the principle of his method depending on the cataphoretic effect of the electric current on charged colloidal particles. In considering the properties of colloids it was found that most of them were charged either

positively or negatively and could be collected at the negative or positive pole when a current was passed through a solution of the colloid. The Cottrell process has not only served its purpose in eliminating smoke, but annually saves many dollars by collecting in the same process, valuable products which would otherwise pass into the atmosphere as smoke.

CLAYS AND CERAMICS

Chemically, clays are mixtures of hydrated aluminum, iron, alkali and alkaline earth silicates with varying quantities of feldspar, sand, mica and organic matter. Each clay particle is more or less protected by colloidal inorganic substances such as silica, hydroxides of iron and aluminum, as well as colloidal organic matter commonly known as humus. The amount of inorganic matter in the colloidal state varies from 0.5 to 1.5 per cent. If too little is present the clay is called weak, lean and sandy, and has a low plasticity. On the other hand a large amount of inorganic colloids makes the clay fat, strong and sticky instead of plastic. A clay suitable for modeling or ceramic manufacture, necessitates therefore, a proper relation between the proportions of colloidal and granular matter.

The extent of colloidal matter in clays determines not only the plasticity, but is also the important factor in shrinkage and cracking of ceramics during the process of firing. Clays high in colloidal material shrink more than those low in this constituent and also crack more easily on being dried. The incorporation of granular matter increases the strength of the ware by reducing the shrinkage and preventing to a considerable extent the formation of these cracks. Frequently highly colloidal clays are pre-heated before mixing to dehydrate the colloidal matter which does not immediately become rehydrated on the addition of water during the mixing.

GEMS AND MINERALS

Some of the costliest members of the mineral kingdom owe their beauty to minute quantities of colloidal particles of coloring matter dispersed in them. The color of the ruby is due to colloidally dispersed iron, that of the sapphire to colloidal cobalt oxide, while the emerald owes its color to chromium. Opal is itself a colloid with interior reflecting planes. Mother-of-pearl has been made artificially by precipitating colloidal calcium carbonate under definite conditions. Agates and jaspers are examples of minerals formed by a process of rhythmic precipitation

in a colloidal gel. In order to show how these agate formations may be imitated in the laboratory the following experiment may be performed. A gelatin solution of potassium dichromate is prepared and allowed to harden. The solid mass is then transferred to a somewhat larger container filled with a solution of silver nitrate and allowed to stand for about twenty-four hours. The silver nitrate is poured off, the gelatin rinsed with water and then cut into sections. Upon examination the gelatin is seen to be streaked with numerous concentrically arranged bands of silver chromate strikingly similar to the banding in agates and jaspers. The formation of the bands is the result of the diffusion of the silver nitrate solution into the gelatin until a point is reached where the concentration of dichromate is sufficient to precipitate silver chromate. This diffusion progresses and at each point where sufficient dichromate is present to form silver chromate a precipitate is formed.

Colloidal metals and colloid metallic compounds are much used to give color to various glasses. Ruby glass owes its red color to the presence of colloidal gold particles. Silver, colloidally dispersed in glass, colors it yellow or brown. Selenium imparts a red or violet depending on the size of the particles. The influence of particle size on the color produced may be shown very nicely with colloidal solutions of gold. Solutions of extremely fine colloidal gold particles are red in color, while solutions of larger particles display a blue color.

ICE CREAM AND CONFECTIONERY

The importance and value of protective colloids is strikingly demonstrated in the manufacture of ice cream. Those who have had experience in the preparation of this article of food realize that the quality and texture of the final product depends on the addition of some protective colloid such as egg or gelatin. The purpose of the addition is twofold: first, to prevent the crystallization of the water as small particles of ice which make the ice cream gritty and rough, and second, to stabilize or protect the casein which otherwise would form difficultly digestible curds.

The impression is common that gelatin in ice cream is used as a filler in order to cheapen the cost of production. Actually gelatin is expensive and the quantities used are so small that such a possibility is precluded.

Candies of all kinds are made with the addition of some protective colloid such as gum arabic, soluble starches, glucose or certain

gums. The colloid prevents the crystallization of sugar and gives the candy a smooth body. A super-dried starch containing only a few per cent. of moisture is used in molding candies to absorb moisture and thereby keep the candy in shape. Pectin in jellies and jams acts as a protective colloid in preventing the crystallization of sugar.

PAINTS AND PIGMENTS

Previously it has been shown that the color of gold solutions depends on the size of the individual gold particles. A similar condition exists in the case of paints where the degree of subdivision of the pigment particles determines not only the color, but also the covering power and opacity of the paint. The color of lead chromate, a commonly used pigment, may be either yellow or orange depending on the size or degree of dispersion of the individual particles. Although coarsely ground pigments are avoided in paint manufacture, it is quite as important not to obtain too fine a pigment as undesirable properties are introduced as subdivision increases beyond a certain optimum point.

It is interesting to note the effect of certain foreign substances which are added during the process of paint manufacture. E. G. Acheson has pointed out that small quantities of tannic acid cause a pigment to deflocculate readily on grinding in oil. The emulsification of a small quantity of water in mixed paints has the effect of preventing settling and hardening of the pigment in the can.

RUBBER

The study of the physical and chemical properties of rubber has advanced considerably as a result of developments in colloid chemistry. Caoutchouc, the fundamental substance from which commercial rubber is made is a typical colloid and is obtained in the sap of certain trees or shrubs. Normally the sap or latex as it is known, is a milk-like fluid differing somewhat in its properties according to the origin, chemically it consists of a watery liquid in which are dispersed globules of caoutchouc. In order to prepare rubber it is necessary to coagulate the caoutchouc. This may be done by evaporation, smoking or by adding certain reagents which change the physical condition of the film of protein which protects each globule of caoutchouc. The problem of choosing the best means of coagulation is complicated by the presence of either protein or peptone protective colloids in the latex.

It is of interest to note that rubber particles are now being electrically deposited directly from the latex, on metal or ceramic molds.

Sulphur, as well as fillers such as zinc oxide, carbon black, etc., may be incorporated in the latex and all deposited on the positive pole.

The process of vulcanization depends on the combination of sulphur with rubber. The first stage of this combination seems to consist of the adsorption of the sulphur by the rubber which on heating probably forms a true chemical combination. The wearing qualities of rubber also depend on the nature of the various fillers which are used and it has been conclusively demonstrated that the finer the particles of the filler the better the wearing quality of the rubber.

ADSORPTION

The adsorption of gases and vapors by certain porous bodies such as charcoal and kieselguhr has long been a matter of common knowledge. All of us are familiar with the use of charcoal as an adsorbent of foul odors as well as of poisonous gases. This property of charcoal is not limited to adsorption of gases, but has been extended to the adsorption of various substances from solutions, notably the decolorizing action of activated charcoals.

Silica gel prepared from the coagulation of a colloidal solution of silicic acid is likewise an excellent adsorbent. The word gel does not accurately describe its physical nature, but rather indicates its condition at one stage of its manufacture. As actually used it is a hard glassy material, with the appearance of clear sand and having the formula SiO_2. The property which differentiates it from ordinary sand, however, is its highly porous structure and especially the size and uniform distribution of these pores. Silica gel may be pictured as a piling up of billions of little balls of clear sand one on top of the other, which, if they could be seen, would probably resemble a pile of cannon balls or marbles. Between these little spheres are billions of spaces or pores which create a tremendous capillary attraction. It is said that four pounds of water can be put on ten pounds of silica gel and the water will be sucked in instantly, while the silica mass will remain dry and not increase in volume. The variety of uses to which silica gel has been put as an adsorbent is amazing. Thus, sulphur compounds are separated from petroleum by the selective adsorption of the former by silica gel. Blast furnace air is deprived of its moisture by the dehydrating effect of silica gel. Silica gel is used in toilet powders as an adsorbent for perspiration and under certain conditions silica gel also acts as an adsorbent for foul odors. The latter property may be demonstrated by passing the vapors emanating from Limburger cheese through a tube containing activated silica gel, abso-

lutely no odor being detectable at the outlet of the tube. The process of activating the gel consists of heating it at 150 deg. C. for two hours, while a current of dry air is passed through the tube. This operation reduces the moisture content of silica gel to a minimum.

INCANDESCENT LAMPS

An interesting application of colloid chemistry is the use of metals in colloidal subdivision in the manufacture of incandescent light filaments. For a long time trouble was experienced in obtaining tungsten and tantalum and other metals in the form of filaments because of the brittleness of the metals. To overcome this difficulty the metals were finely subdivided and then made into pastes, frequently with the addition of some organic colloid which could be easily hydrated. The pastes were then squeezed through fine openings to form threads or filaments of the metals.

IRON, STEEL AND ALLOYS

The brittleness of cast iron and the strength of various steels are facts commonly known. An examination of these substances reveals the coarsely crystalline structure of cast iron compared to the microscopic nature of the finer grades of steel. One of the axioms of metallurgy is that the smaller the "grain" or crystal size, the better and stronger the product. Crystal size in alloys depends to a great extent on the rate at which freezing of the molten alloy is allowed to take place, rapid freezing producing small crystals, slow freezing large ones. The grain size varies also with the composition. For example, traces of various metals added to alloy steels has the effect in many cases of producing a fine grained alloy possessing great strength. It is reported that vanadium in steel reduces the size of ferrite grains and makes the pearlite structure fine grained and homogeneous, thereby producing a harder steel. Colloid chemists are of the opinion that fine grained structures in metals are caused by the inhibition of crystallization by colloidally dispersed substances. Molybdenum, chromium, vanadium, tungsten and nickel are elements which are much used in the manufacture of fine grained alloy steels.

CONCLUSION

With this brief presentation of the theory and a few of the practical applications of colloid chemistry the scope of the subject has by no means been exhausted. A complete story of colloids would also include such diversified subjects as photography, tanning, paper manufacture, sewage disposal, ore flotation,

lubrication, soap manufacture, fabric shower-proofing, foods and food preparation, chemical analysis, agriculture, colloidal fuels, etc. Indeed there are probably very few technical operations and substances which in one phase or another have no connection with colloids or colloid chemistry.

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QUINCE SEED OIL

By W. H. Dickhart

DURING Civil War times the young ladies took just as much pride in keeping their hair and hands trim as our modern girls. To accomplish this, they were compelled to make their own lotions, for they could not go to a nearby drug store and purchase one of any number of hair and hand lotions, such as we have now on the market. Therefore, when the quince preserving season arrived they would save the quince seeds, dry and store them for future use. Then, whenever they desired a lotion they would place some of the seeds in a container with water, boil them for ten minutes and strain the hot mass into a suitable receiver through a piece of muslin, thus separating the liquid from the shells and broken seeds. After permitting the liquid to cool, a jelly mass was formed which they would apply as such as a hair dressing, with very satisfactory results. Diluted with water, it furnished a hand lotion.

Since that time we have learned a little more about Cydonium (quince seeds) and the present commercial supply, according to Kramer,[1] is chiefly from Southern Russia and Portugal single or in agglutinated masses. The seeds[2] are ovate angled, reddish-brown externally, white within, inodorous, and nearly insipid, being slightly bitter when long chewed. They contain[3] about 22 per cent. of mucilage yielding on hydrolysis oxalic acid and forming, arabinose on treatment with dilute sulphuric acid.

Two drachms[4] of the seeds will render a pint of water thick and ropy (*A. J. P.*, 1876, 35). In preparing the mucilage the U. S. P. of 1880 gave the following formula, "Cydonium—Two parts—Distilled water 100 parts. Macerate the Cydonium for half an hour in a covered vessel, drain the liquid through muslin without pressure. The preparation should be freshly made when required for use."

The mucilage when dried had an odor of rose leaves. The powdered meal left after the oil had been extracted with petroleum ether gave, when mixed with water, an odor resembling benzaldehyde.

The seeds also contain[5] about 15 per cent. of a fixed oil, amygdalin, tannic acid, a coloring matter and 13 per cent. ash. After extracting some dry seeds with petroleum ether the extracted oil gave the following characteristics:

Specific Gravity at 15°	0.9251
Iodine Value (Wijis)	112.4
Saponification Value	187.6
Index of Reference at 40° c.	1.4696
Index of Reference at 40° c. of the fatty acids	1.4639
Unsaponifiable matter	9.35%
Free fatty acid (as oleic)	6.49%
Iodine Value of Fatty Acids	100.5
Total Fatty Acids	90.4%
Halphen Test	Negative
Villavechia Test	Negative
Bellier Test	Trace

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ABSTRACTED AND REPRINTED ARTICLE

THE STANDARDIZATION OF CHEMICAL NOMENCLATURE*

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In addition to the reporting of some new rules relating chiefly to the written form of the names of organic compounds, this article includes the more important other general rulings pertaining to accepted nomenclature standards and a classified list of references to sources of information thought likely to be helpful in guiding present-day usage. Further work now actively in progress is mentioned.

The number of chemical words is very large. There are so many compounds to be named. In the pronunciation, spelling, and written form of these words much variation is to be found. It would be well if greater uniformity could be obtained. Exactness is important in stating chemical information just as it is important in the chemical laboratory and there are pedagogic as well as cultural advantages in uniform good usage. Certain standards have been set up and further work in this direction is being done each year. An effort will be made here to give the more important general rulings, to tell where other information can be found and to mention briefly the further work now actively in progress.

Pronunciations

There is no authoritative standard for chemical pronounciations. The dictionaries differ. An effort to set up some standards is being made now by the Committee on Nomenclature, Spelling, and Pronunciation of the American Chemical Society and it is planned to publish a report as soon as possible.

Nomenclature Rules

It is not the purpose here to trace the history of the development of modern chemical nomenclature but merely to give information

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†Chairman of the Committee on Nomenclature, Spelling, and Pronunciation of the American Chemical Society.

thought likely to be helpful in guiding present-day usage. There are still many disputed points; only matters which seem to be pretty definitely settled will be considered.

The nomenclature committees of the International Union of Chemistry, in particular the committee for organic chemistry, have made considerable progress in the formulation of guiding rules but final decisions have been delayed, partly because the obtaining of international agreement is naturally a slow process and partly because of a desire to permit German chemists, who were not represented until recently, to participate in the undertaking.

In 1923 the Nomenclature Committee of the British Chemical Society and that of the American Chemical Society agreed on ten rules covering some of the more commonly disputed points. Some of these relate to endings which have a classification significance. These rules follow:

1. In naming a compound so as to indicate that oxygen is replaced by sulfur the prefix *thio* and not *sulfo* should be used (sulfo denotes the group SO_3H); thus, HCNS, *thio*cyanic acid; H_3AsS_4, *thio*arsenic acid; $Na_2S_2O_3$, sodium *thio*sulfate; $CS(NH_2)_2$, *thio*urea. They only use of *thio* as a name for sulfur replacing hydrogen is in cases in which the sulfur serves as a link in compounds not suitably named as mercapto derivatives; thus, $H_2NC_6H_4SC_6H_4NH_2$, thiobisaniline. *Hyposulfurous acid,* not hydrosulfurous acid, should be used to designate $H_2S_2O_4$.

2. The word *hydroxide* should be used for a compound with OH and *hydrate* for a compound with H_2O. Thus, barium hydroxide, $Ba(OH)_2$; chlorine hydrate, $Cl_2 \cdot 10H_2O$.

3. Salts of chloroplatinic acid are *chloroplatinates* (not platinichlorides). Similarly salts of chloroauric acid are to be called *chloroaurates.*

4. Hydroxyl derivatives of hydrocarbons are to be given names ending in *-ol,* as glycer*ol,* resorcin*ol,* pinac*ol* (not pinacone), mannit*ol* (not mannite), pyrocatech*ol* (not pyrocatechin).

5. The names of the groups NH_2, NHR, NR_2, NH, or NR should end in *-ido* only when they are substituents in an acid group, otherwise in *-ino;* thus, MeC(:NH)OEt, ethyl im*ido*acetate; $H_2NCH_2CH_2CO_2H$, β-am*ino*propionic acid (not am*ido*propionic acid); $PhNHCH_2CH_2CO_2H$, β-anil*ino*propionic acid; $CH_3C(:NH)CO_2H$, α-im*ino*propionic acid.

6. Hydroxy-, not oxy-, should be used in designating the hydroxyl group; as *hydroxy*acetic acid, $HOCH_2CO_2H$, not *oxy*acetic acid. *Keto-* is to be preferred to *oxy-* or *oxo-* to designate oxygen in the group —CO—.

7. The term *ether* is to be used in the usual modern acceptation only and not as an equivalent of *ester.*

8. Salts of organic bases with hydrochloric acid should be called *hydrochlorides* (not hydrochlorates nor chlorhydrates). Similarly hydrobromide and hydroiodide should be used.

9. German names ending in *-it* should be translated *-ite* rather than *-it,* as permut*ite.* If it seems desirable to retain the original form of a trade name it should be placed in quotation marks, as "Permutit." Alcohols such as dulcitol (German Dulcit) are exceptions.

10. German names of acids should generally be translated by substituting *-ic acid* for *"-säure."* Some well-established names are exceptions, as Zuckersäure (saccharic acid), Milchsäure (lactic acid), Valeriansäure (valeric acid), etc. For a few well-established names it is correct to translate "-insäure" *-ic acid* instead of *-inic acid. E. g.,* Acridinsäure is acridic acid. Names ending in "carbonsäure" are to be translated *-carboxylic acid* (not *carbonic acid*).

The Written Form

Conflicting usage is very common in the written form of organic names in that some use a single word without hyphens, as *phenyldiethylcarbinol,* some hyphenate, thus *phenyl-diethyl-carbinol,* and others split such names into parts, thus *phenyl diethyl carbinol.* It is considered good practice to limit the use of hyphens in organic names to the attachment of position numbers and symbols and the like, as *1-sec-butyl-4-iodobenzene* and *a-amino-m-toluic acid.* Some chemical names are properly single words and others are properly made up of two or more separate words. In an effort to help bring about better uniformity in practice in this respect and to provide other information useful in name construction, the following rules have been prepared, after careful study, by a committee of organic chemists named jointly by the Division of Organic Chemistry and the Division of Chemical Education of the American Chemical Society. The work was done under the active leadership of Charles D. Hurd. They have been approved by the American Chemical Society's general nomenclature committee and were adopted as official

standards by the Council of the Society at its meeting in Indianapolis, March 30, 1931.

1. When a hydrogen atom of a compound is substituted by another atom or group, the name of this compound may be retained as the root of the name for the substituted compound. In such names, the prefix (denoting the substituent) is to be directly attached to the root and not spaced from it.

The position of monosubstituents is never labeled with compounds whose replaceable hydrogens are all equivalent, as methane, acetylene, benzene, ketene, hydrazine, carbinol, acetic acid, glyoxylic acid, acetone, arsine, etc. With compounds which contain more than one type of replaceable hydrogen, such as toluene, aniline, propionic acid, benzoic acid, hydroxylamine, acetophenone, furan, etc., ambiguity is avoided by labeling the position of substitution with numerals or with such labels as ortho or *o*-, meta or *m*-, para or *p*-, alpha or α-, omega or ω-, etc.

Examples:

diphenylmethane	and not	diphenyl methane
phenylacetylene	and not	phenyl acetylene
chlorobenzene	and not	chloro benzene
dimethylketene	and not	dimethyl ketene
phenylhydrazine	and not	phenyl hydrazine
phenyldiethylcarbinol	and not	phenyl diethyl carbinol
2-methyl-2-hexanol*	and not	2-methyl 2-hexanol
or		
methyl-2-hexanol-2	and not	methyl-2 hexanol-2
or		
2-methylhexanol-2	and not	2-methyl hexanol-2
o-chlorophenylacetic acid	and not	*o*-chlorophenyl acetic acid
Methylallene	and not	methyl allene
2,4,6-tribromophenol	and not	2,4,6-tribromo phenol

1*a*. "Amine" is regarded as a contraction of "ammonia," and thus is used as the root to which the names of the substituents are directly attached as prefixes. This makes for uniformity with "arsine," "aniline," "hydrazine," etc., and distinguishes it from such

*Whether the numerals should be "fore" or "aft" or "fore and aft" is at present a debatable question.

names as alcohol, ether, or ketone which only represent types. Thus, methylamine is preferred to methyl amine, ethylenediamine to ethylene diamine, triphenylarsine to triphenyl arsine, *N,N*-dimethylaniline to *N,N*-dimethyl aniline and *p*-tolylhydrazine to *p*-tolyl hydrazine.

2. Since there is no definite unsubstituted compound which is designated by *alcohol, ether,* or *ketone,* these terms are always used as separate words.

Examples:

ethyl alcohol
n-butyl alcohol
dimethyl ether
ethyl methyl ether and not ethylmethyl ether
dimethyl ketone
ethyl methyl ketone and not ethylmethyl ketone
p-bromophenyl *m*-tolyl ketone

3. If two words are used in naming *aldehydes* or *nitriles,* the first word is the same as the first word of the name of the corresponding acid. If, as is usually the case, one word is used for these names, the first word of the name of the acid is suitably altered to become a prefix. Usually, this alteration is a detachment of *ic* for aldehydes, as acetaldehyde, propionaldehyde, contractions of acetic aldehyde and propionic aldehyde, respectively. However, in naming benzaldehyde, *oic* has been detached. With nitriles, an *o* is usually introduced for euphony, as acetonitrile and butyronitrile, but the contraction may go back to an *o* as propionitrile.

4. Isocyanate is a separate word. Thus, C_6H_5NCO is phenyl isocyanate. This practice is correct for esters in general.

5. In naming metallo-organic compounds, the alkyl groups should precede and be directly attached to the name of the metal. Thus, methylmercuric iodide, diethylzinc, ethylmagnesium bromide, tetraethyllead, tetramethylgermanium, etc.

6. It is recommended that in aliphatic unsaturated compounds, the use of the delta be discontinued.

Examples:

3-Buten-1-ol, $CH_2(OH)CH_2CH:CH_2$ instead of Δ^3-1-butenol

1-Penten-3-one, $CH_2:CHCOCH_2CH_3$ instead of Δ^1-3-pentenone

2,4-Pentadien-1-ol, $HOCH_2CH:CHCH:CH_2$ instead of $\Delta^{2,4}$-1-pentadienol

3-Hexene-2,5-diol, $CH_3CH(OH)CH:CHCH(OH)CH_3$ instead of Δ^{3}-2,5-hexenediol

4-Heptene-2,3,6-trione, $CH_3COCOCH:CHCOCH_3$ instead of Δ^{4}-2,3,6-heptenetrione

2,5,7-Octatrien-4-one, $CH_3CH:CHCOCH:CHCH:CH_2$ instead of $\Delta^{2,5,7}$-4-octatrienone

It is our very strong hope that chemists in general and editors and publishers in particular will follow these new rules. This applies to the other rules, too, but they are much better established in usage.

References

There is no one place to which interested chemists can turn for full information on chemical nomenclature. It is not feasible to assemble here all of the rulings and forms established as standards but references can be given to the sources considered most useful for such an inquiry.

For *listed names of individual compounds and elements* see—

(a) The Second Decennial Index in *Chemical Abstracts* or any recent annual subject index.*
(b) The subject indexes to *British Chemical Abstracts.*
(c) Webster's "New International Dictionary" (for the commoner compounds).
(d) Hackh's "Chemical Dictionary."
(e) The index to Roscoe and Schörlemmer, "A Treatise on Chemistry" (for inorganic compounds).
(f) The indexes to the various volumes of Mellor's "Comprehensive Treatise on Inorganic and Theoretical Chemistry" (for inorganic compounds).
(g) Dorland's "The American Illustrated Medical Dictionary," 15th edition.
(h) The index to the American Medical Association's "New and Nonofficial Remedies" (for medicinal substances).

For *organic ring systems* see—

(a) Patterson: *J. Am. Chem. Soc.*, 47, 543-61 (1925); 50, 3074-87 (1928).
(b) The Ring Index which is a part of the introduction to the subject index to *Chemical Abstracts* for each year since 1916.
(c) Stelzner: "Literatur-Register der organischen Chemie," 5, ix-xv (1926).

*In building the indexes to *Chemical Abstracts* special care has of necessity been used to observe what is considered best usage in nomenclature. These indexes are naturally comprehensive and extensive and accordingly reference is made to them and accompanying compilations, the hope of extending their usefulness having been allowed to outweigh reluctance to speak of the work of my own office as standard.

For the *names of organic radicals* see—

The Introduction to the subject part of the first and second decennial indexes to *Chemical Abstracts* and that to the 1927 annual index of the same journal. These lists are complete to date, a few additions are listed each year in the annual indexes.

For the *Geneva system* of naming organic compounds (many of the Geneva names are now not commonly used) see—

Pictet: *Arch. sci. phys. nat.* [3], *27*, 1-36 (1892).
Tiemann: *Ber.*, *26*, 1595 (1893).
For examples see Beilstein's "Handbuch der organischen Chemie," 4th edition, in which Geneva names are used systematically.

For a *discussion of organic nomenclature* with particular reference to names for indexing see—

(a) Patterson and Curran: *J. Am. Chem. Soc.*, 39, 1623-38 (1917).
(b) The Introduction to any subject index to *Chemical Abstracts* published since 1916, where the discussion is brief.

For the *rules under consideration by* the nomenclature committees of *the International Union of Chemistry* see—

(a) Biochemistry:
Bull. soc. chim. biol., 5, 95-109 (1923).
Ibid., 8, 1211-6 (1926).
Bull. trimestr. assocn. élèves école sup. brasserie univ. Louvain, *27*, 139-43 (1927).
Bull. soc. hyg. aliment., 16, 277-82 (1928).
Schweiz. Apoth. Ztg., 66, 193-7 (1928).
(b) Inorganic chemistry:
Ind. Eng. Chem., 18, 320-1 (1925).
Chem. Weekblad, 23, 86-99 (1926), (in English).
Bull. soc. chim., 43, 289-300 (1928).
Gazz. chim. ital., 58, 883-91 (1928).
Rec. trav. chim., 48, 652-63 (1929).
(c) Organic chemistry:
Ind.-Eng. Chem., 18, 321-3 (1926).
Rec. trav. chim., 48, 641-51 (1929).

For *reports of the American Chemical Society's Nomenclature Committee* on specific problems, as the naming of pectic substances, see—

Proc. Am. Chem. Soc. (These reports are made each year at the spring meeting and usually appear in the *Proceedings* part of the May number of *J. Am. Chem. Soc.*)

For *miscellaneous articles or parts of articles on nomenclature* see—

Chemical Abstracts subject index entries under the heading *Nomenclature.*

MEDICAL AND PHARMACEUTICAL NOTES

DIGITALIS, COLORIMETRIC ASSAY OF. B. J. Ockeloen and J. C. Timmers. (*Pharm. Weekbl.*, 1931, **68**, 820.)—As the authors had available a large number of samples of physiologically standardised digitalis, they took the opportunity of comparing them by the colorimetric method of Knudson and Dresbach. This is carried out by precipitating the infusion first with lead acetate, then with sodium phosphate. The filtrate is treated with sodium picrate, and the color obtained compared with that given by a standard solution of ouabaine. In place of the latter the authors used a solution of potassium dichromate standardised against thiosulphate. The following results were obtained:

		——*Focke units*——	
	C.c. 0.1 N thiosulphate	*Colorimetric*	*Physiologically determined*
D. ambigua	33.8	8.9	8.81
D. ambigua	30.8	8.1	7.6
D. ambigua	28.8	7.3	7.03
D. lanata	64.9	17.1	18.16
D. lutea	21.3	5.6	5.40
D. lutea	19.8	5.2	5.28
D. lutea	15.5	4.1	4.36
D. purpurea	30.0	7.9	7.96
D. purpurea	17.8	4.7	4.56

With high values, as with *D. lanata*, a longer time should be given before the colors are compared, and the test should be repeated with a weaker infusion. These results are not in agreement with those of other investigators, who have stated that the results of the colorimetric method are not comparable with those of the physiological method. It has been stated that this is due to the color being produced solely by the sugars present. Experiments of the authors show that sugars in general do not give much color in cold solutions, though unfortunately they were not able to test digitoxose as no sample was available. The

strongest reaction among the sugars was obtained with ketoses. They conclude that it is possible that digitoxose gives a positive reaction. The method of Martindale and Westcott was also tested, but no comparable results could be obtained as the non-official varieties of *Digitalis* gave colors which were entirely different from those given by *D. purpurea.*—(*G. M., Quart. Journ. of Pharm.*, **5**, 82.)

PYRETHRUM, CHEMICAL METHODS OF EXAMINATION OF. J. Ripert. (*Ann. Falsif.*, 1931, **24**, 325.)—The toxicity of pyrethrum is due to pyrethrins 1 and 2, which are esters of a ketonic alcohol, pyrethrolone, and chrysanthemum mono- and dicarboxylic acids respectively. That it is due to these esters, as such, is shown by the disappearance of toxicity on hydrolysis. No method of extraction of the pure esters, a true measure of the toxicity, is available; crystalline semicarbazones of the pyrethrins can be obtained, but the yield is not quantitative. The methods of examination, at present available, are based on the determination of the two acids or of pyrethrolone. Staudinger, Ruzicka and Harder proposed the first method for the determination of the acids. The drug is extracted with petroleum ether. The residue, after removal of the solvent, is extracted with eight portions of warm methyl alcohol. Each extraction is cooled to 0° C. and the precipitated fatty acids separated by filtration. The combined filtrates are diluted with 10 per cent. of their volume of water, cooled to 0° C., allowed to stand for two hours and again filtered. The monocarboxylic acid in an aliquot portion of the filtrate is separated by addition of acid and steam distillation. The acid in the distillate is extracted with petroleum ether and determined by saponification with alkali. The dicarboxylic acid, which is not volatile in steam, is extracted from the aqueous residue with ether and determined by saponification. The author finds the value obtained for this second acid is not true. There is present in the aqueous residue an acid soluble in petroleum ether, a solvent in which the dicarboxylic acid is not soluble; this acid is probably a fatty acid. The aqueous residue should be treated with petroleum ether prior to extraction with ether. Other authors have adopted this method of Staudinger, Ruzicka and Harder, simplified by the omission of the separation of fatty acids, as a measure of the value of pyrethrum. As, however, the fatty acid

content of the drug shows considerable variation, this simpler method is considered valueless. The determination of pyrethrolone, as semicarbazone, presents difficulty. Although a crystalline semicarbazone can be obtained from pure pyrethrolone, whatever method is employed for the hydrolysis of the pyrethrins no pyrethrolone is obtained, but an acid, viscous, ill-defined body. Staudinger and Harder proposed a method based on the formation of the semicarbazones of the pyrethrins. To 50 c.c. of the methyl alcoholic solution of pyrethrins, as obtained in the acid determination, is added 1.2 gm. of semicarbazide hydrochloride and 1.2 gm. of sodium acetate in 8 c.c. of water. After allowing to stand for twenty-four hours, the methyl alcohol is removed by aspiration, the residue washed with five portions of 100 c.c. of water, the residue dissolved in ether and again washed with water. After removal of the ether, the nitrogen content of the semicarbazone residue is determined by the Kjeldahl method, using fuming sulphuric acid, phosphorus pentoxide and mercury as catalyst. Similar methods, employing different means for the determination of the semicarbazones have been proposed. Hydrolysis with acid, oxidation of the hydrazine formed with alkaline mercuric chloride solution and collection of the nitrogen; oxidation of the hydrazine with iodic acid to ammonia and determination of the latter; titration of the hydrazine with potassium iodide, etc. The results from these methods do not agree with those from the acid method, higher values being obtained. Attempts to make use of the reducing powers of pyrethrolone by applying the methods of Folin and of Hagedorn and Jensen also gave high results as compared with those from the acid method. The author by a careful examination of the carbazones, obtained from the crude extract and from the extract purified with methyl alcohol by various methods, isolated a carbazone of a methyl ester of pyrethrolone. The ester was found to be present in the drug in the free state. It is due to the presence of this compound that the pyrethrin content, calculated from the results of the reduction or semicarbazone methods, is higher than that from the determination of the acids; moreover, as the ester possesses no toxicity these higher results are not a measure of the value of the drug. Samples of the drug from different sources all gave evidence of the presence of this ester; the content varied from 1 to 4 gm. per kgm. Further examination of the carbazones obtainable is required before a chemical method for the determination of the pyrethrins in pyrethrum can be formulated.—(*B. W. M., Quart. Journ. of Pharm.*, 5, 97.)

ROTENONE—Determination of the complete chemical structure of rotenone was announced recently by Dr. C. A. Browne, Assistant Chief of the Bureau of Chemistry and Soils, U. S. Department of Agriculture, who explained that chemists of the department hope that rotenone can be developed ultimately into the insecticide most nearly approaching the ideal.

With a knowledge of the structure of rotenone and associated compounds, said Doctor Browne, it will be possible to attempt to synthesize rotenone as a chemical product instead of being forced to extract it from vegetable sources. This new knowledge may also permit the synthesis of other compounds of analagous make-up which are likely to possess valuable insecticidal properties.

"Chemists of the bureau have been in keen competition with some of the best chemists in Japan and Germany," says Dr. Browne. "By solving this difficult problem ahead of those who started many years earlier, our chemists have earned credit for one of the most brilliant chemical achievements of the department."

Dr. F. B. LaForge, Dr. H. L. Haller and L. E. Simth were named by Doctor Browne as the scientists who accomplished this discovery. It is expected that further investigation will result in the production of insecticides which will be more effective in checking the ravages of insect pests which cause tremendous losses each year in this country.

Rotenone is a white crystalline material, and is both a contact insecticide and a stomach poison. It is more poisonous to aphids (soft-bodied plant lice) than is pure nicotine. It is also poisonous to fish and other cold-blooded animals, but appears to have no effect on humans and warm-blooded animals, a property which adds greatly to its usefulness. It can be obtained from the roots of *Derris elliptica,* an East Indian plant, and also from the roots of *Lonchocarpus nicou* or cube (pronounced coo-bay) from South America. This species of derris is a vine, and is a member of the pea family. Cube is a shrub-like plant resembling a small common locust tree.

SUCCESSFUL USE OF NEW GERMAN TEST FOR CANCER REPORTED—Cancer, it is claimed, can be detected by a serum reaction discovered by Dr. H. J. Fuchs of Berlin. The reaction is based on the fact that fibrin from the blood of a person without cancer is broken down or digested by the serum of the blood of a person with cancer, with the production of some nonprotein nitrogenous substances which can be detected by suitable chemical means.

The method as it was described by Dr. Fuchs required special apparatus and some special training for the observer, which tend to prevent its general use.

Prof. M. von Falkenhausen of the University of Breslau, Germany, now reports a simplification of the method that may make it possible for other observers to test its validity. He has introduced into the reaction a colorimetric procedure which he states makes the method more exact and at the same time much simpler to carry out. He reports a series of eighty cases in which the reaction was used and in which there was not a single failure in the diagnosis. In some of the cases the reaction was negative and in these subsequent surgical operation or medical treatment established the correctness of the diagnosis.

Prof. von Falkenhausen gives a preliminary description of his method in the *Deutsche Medizinische Wochenschrift* and promises a fuller paper later. He believes that his method will be of great assistance to physicians in the campaign against cancer.—(*Science Service.*)

Warning Against Thallium Poisoning—The metal thallium, is apparently a dangerous poison. Therefore its use in human medicine and in wholesale poisoning activities against rodents and other lower forms of life should be restricted until more is known about its action and the habits of the animals against which it is used, warns Dr. Marcus Ward Lyon, Jr., in a note in the current issue of *Science*. Similar warning against the use of thallium as a rat poison has recently been issued by the American Medical Association.

Numerous deaths have followed the use of thallium as a depilatory for cosmetic purposes and the treatment of ringworm of the scalp, Dr. Lyon points out. Several fatal cases of thallium poisoning have also been reported from the use of thallium-poisoned grain for the destruction of ground squirrels. Thallium is also poisonous to plant life.

"The amount of thallium distributed in poisoned grain for destroying rodents and other forms of life is quite appalling," declares Dr. Lyon.

He questions whether there is any likelihood of the thallium-treated grain being placed in the same situation year after year, such

as might happen if old burrows are occupied by incoming ground-squirrels. In that case, he suggests there would be danger of causing patches of soil sterility.

Thallium was discovered by Sir William Crook in March, 1861, while he was looking for another element, tellurium, in a flue-dust of roasted seliniferous pyrites. The new element was supposed to belong to the sulfur group until 1862 when Lamy of Lille isolated it, showed it to be a metal, and described its properties.

During his study of thallium, Lamy experienced weakness and pains in the legs which made him suspect it of being poisonous. He showed that this was the case by studying its effects on animals. It was later found useful in treating colitis and tuberculosis, and in this connection its depilatory effect was accidentally discovered when the patients' hair began falling out. Besides total loss of hair, thallium poisoning may produce such symptoms as weakness, pains in the legs, neuritis, mental disturbances, kidney involvements, excess salivation, heart palpitation and visual disturbances.

In the latter cases, phsicians were at a loss to explain the blurring and loss of vision, until they accidentally found that a thallium depilatory had been used by all the patients. When this was discontinued the vision improved.

Studies by the Bureau of Investigation of the American Medical Association of the depilatory implicated in the poisonings showed that it contained over 7 per cent. of thallium acetate, whereas Raymond Sabouraud, one of the first to use thallium for removing hair, warned against using it in any stronger concentrations than 1 per cent.

The sale of this depilatory has recently been prohibited in San Francisco.—(*Science Service.*)

New Commercial Products from Cane Sugar—Organic chemists are very much given to the practice of preparing various substances, studying their properties and moving on to other fields. In this way several hundred thousand compounds have been prepared, their properties reported in chemical journals, and the substances themselves stored in dusty bottles on forgotten shelves.

Occasionally some of these creations are dragged forth and examined for usefulness. Such is the case of some compounds that may be made from ordinary cane sugar. In a paper read before the

Sugar Division of the American Chemical Society at New Orleans, on March 29, 1932, Drs. Gerald J. Cox and John Metschl, of Mellon Institute of Industrial Research, Pittsburgh, Pa., have described some of their studies on materials made from sugar.

They have found that sucrose octa-acetate, which was first prepared in 1865, may find a useful place in modern lacquers. It is a resinous material which, when compounded with other materials, serves as an adhesive. It has also been employed in treating paper. Sucrose benzoate, another compound of sugar that has been known for many years, may find similar uses.

When sugar is treated with hdrochloric acid at a temperature somewhat higher than that of boiling water, it is converted into acidic substances. One of these acids, levulinic acid, was made and studied forty years ago. When it is properly treated with alcohol, fragrant esters are produced that may find uses as solvents in many fields.

NEWS ITEMS AND PERSONAL NOTES

DR. LAWALL REPORTS ON OPIUM ASSAY METHODS—Dr. Charles H. LaWall, Dean of the Philadelphia College of Pharmacy and Science, who was appointed some months ago as a member of the International Committee of the Health Council of the League of Nations, to study the subject of opium assay methods, and who was at that time appointed as a consultant in Pharmaceutical Chemistry to the U. S. Public Health Service of the Treasury Department so that he could legally import the opium upon which the experiments were to be made, has completed the first assignment of the work and sent in his reports to the chairman, Professor L. Van Itallie of Leyden, Holland.

Other members of this International Committee are Professors H. Baggesgaard-Rasmussen of Copenhagen, Denmark; R. Eder of Zurich, Switzerland; A. Goris of Paris, France; E. Knaffl Lenz, and I. Wasserberg of Vienna. There is also a member representing Great Britain, and one representing Japan.

The standardization of opium assay methods is a key factor in the control of the narcotic derivatives of this drug.

SIR HENRY WELLCOME HONORED AGAIN—The *British Medical Journal,* London, contains the announcement that at a meeting of the Council of the Royal College of Surgeons of England, Lord Moynihan, president, in the chair, the Right Hon. Lord Dawson of Penn, P. C., G. C., V. O., K. C. B., K. C. M. G., Physician to His Majesty the King, and President of the Royal College of Physicians of London, and Sir Henry Wellcome, LL. D., F. S. A., founder of The Wellcome Research Institution, were elected Honorary Fellows of the Royal College of Surgeons.

The Royal College of Surgeons of England is one of the most exclusive scientific bodies in England, and the bestowal of this honor on Sir Henry Wellcome is very exceptional in that aside from members of the Royal Family, Sir Henry is the second person not holding a medical degree upon whom this rare distinction has been conferred, the first and only other recipient being the famous Field Marshal Lord Roberts of Kandahar.

Sir Henry Wellcome is of American birth and a graduate of the Philadelphia College of Pharmacy and Science. He is well known for his world-wide scientific work and extensive pioneer researches in connection with tropical diseases, including the founding of The Wellcome Tropical Research Laboratories at Khartoum on the Upper Nile Regions of the Sudan, Africa. He is also a director of the Gorgas Memorial Institute, Washington, D. C., with its tropical research laboratories at Panama.

British Pharmaceutical Exhibition—The Fortieth Chemists' Exhibition, organized by the *British and Colonial Pharmacist*, will be held in the new hall of The Royal Horticultural Society, Greycoat Street, Westminster, situated in the center of the West End of London, an advantage which cannot be overestimated, particularly where visitors from overseas are concerned. The dates are May 23d-27th. All members of the drug and chemical trades who are in England during the week will receive a cordial welcome on presentation of their professional or business cards.

Progress in Research at Mellon Institute During 1931-32—According to the Nineteenth Annual Report of the director, Dr. E. R. Weidlein, to the trustees of Mellon Institute of Industrial Research, Pittsburgh, Pa., the sum of $722,541 was received by the institution from industrial fellowship donors during the fiscal year ended February 29, 1932. The total amount of money appropriated by donors to the Institute for the past twenty-one years was $8,277,018, all of which was expended in defraying the cost of scientific investigations conducted for these companies and associations. Throughout the year covered by the report seventy-five industrial fellowships, employing 176 scientists and engineers, were in operation. At the close of the year fifty-eight fellowships were active, and of these twenty-eight have been at work for five years or longer and thirteen have concluded more than ten years of research.

In reviewing the progress that has been made since 1911, when the industrial fellowship system was established at the University of Pittsburgh, Dr. Weidlein points out that Mellon Institute has had

fellowships on 230 distinct subjects, on which 775 scientists and engineers have been engaged. In all, during the period 1911-1932, 313 fellows and 357 fellowship assistants of the Institute have completed their services to science and technology in the institution and have entered the fields of industry and education. As trained additions to the forces of manufacturing and teaching, these men, Dr. Weidlein says, constitute the Institute's greatest contribution to humanity.

The fellowship achievements of 1931-32 are summarized in the report, special attention being given to the research advances made by the Air Pollution Investigation, the Multiple Fellowship on By-Product Coke, the Iodine Investigation, the Organic Synthesis Fellowship, the Petroleum Production Fellowship, the Protected Metals Fellowship, the Steel Fellowship, the Sugar Investigation, and the Fur Fellowship. The activities of the Institute's Department of Research in Pure Chemistry are also described.

During the calendar year 1931 members of the Institute made the following additions to the literature: Two books, four bulletins, thirty-nine research reports, and thirty-three other papers. Twenty-two United States patents and thirty-three foreign patents were issued to fellows. Lists of the Institute's publications, 1911-1932, and copies of Dr. Weidlein's report for 1931-32 will be sent gratis to laboratory directors, librarians, and science teachers upon request.

The constructional work on the Institute's new building is said to be proceeding satisfactorily; it is thought that this edifice will be completed and ready for occupancy in the summer of 1933.

ROMANCE OF THE RUBBER INDUSTRY—Portraying the romance of the rubber industry, and the part played in its development by the Goodrich Company, manufacturers of more than 32,000 articles of rubber, The B. F. Goodrich Company has issued its latest publication, "The Wonder Book of Rubber."

After relating discovery of rubber by South American Indians, and tracing slow growth of its use in earlier years, the book turns to description of manufacturing processes. It gives brief, but clear explanation of construction of tires, footwear, rubber sundries, mechanical goods and other products covering the range of American industry.

"This book is not offered as a scientific discussion, but only as a story of rubber manufacture and use of rubber products," foreword declares.

Well illustrated, the pictures range from those taken in the tropical jungle and rubber plantations of the Far East to scenes in the Goodrich vulcanizing "pit" and elsewhere in its factories.

Founding of Goodrich in Akron in 1870 by Dr. Benjamin Franklin Goodrich, Civil War surgeon is related. World-wide activities of Goodrich also come in for discussion, pictures and print telling the story of fabric mills, manufacturing plants in this country and abroad and distribution of products throughout the civilized world. If a copy of this book is desired kindly notify the Public Relations Department, B. F. Goodrich Company, Akron, O.